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STUDIES OF HYPOTHYROIDISM IN CHILDREN

By

HENNING JESPER ANDERSEN

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Translated from the Danish
by
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PREFACE

This study was carried out during my appointment at Dronning Louise's Children's Hospital, Copenhagen. My thanks are due to my then chief, Professor, Dr. med. Oluf Andersen, for encouraging my interest in paediatric endocrinology, and for all his help during the course of my work.

I am grateful to my present chief, Professor, Dr. med. Preben Plum, University Hospital Paediatric Department, for his interest in the present study, and for valuable advice during its preparation.

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Mrs. Birte Ørbye Rasmussen, Medical Secretary, has helped me with part of the investigation and in typing the manuscript, and Miss Kathleen Larkin,

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Last but not least, my wife has been a patient helper in innumerable ways during the preparation of the study.

To all those whose help I have received, I would like to extend my warmest thanks.

All case records and roentgenograms originate from Dronning Louise's Children's Hospital, except where otherwise indicated; I am grateful to the various departmental chiefs for permission to make use of these records.

The investigations were carried out with financial support from Statens almindelige Videnskabsfond, P. Carl Petersens Fond, and The Association for the Aid of Crippled Children, New York. I wish to extend my sincere thanks for this valuable assistance.

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Copenhagen, November 1960.

Henning J. Andersen.

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INTRODUCTION

In this study, *hypothyroidism* will signify all forms of hypofunction of the thyroid gland affecting the growth and development of the child. The designation will be used to describe the clinical picture as observed throughout the whole course of childhood, instead of such terms as congenital and acquired myxoedema, non-endemic cretinism, etc. *Athyrosis* is a term signifying all those cases of hypothyroidism in which it has been impossible to demonstrate functional thyroid tissue by means of radioactive iodine.

Hypothyroidism is among the most common endocrine diseases of children. Its precise incidence is not known, but there are about 15–20 new cases per annum in Copenhagen. The disease is suspected in a far greater number of children, but excluded by subsequent examination. Hypothyroidism can present an apparently capricious picture. In certain cases there is almost mathematical regularity in its manifestation and in its reaction to treatment, while in other cases—especially as far as the mental development of the patients is concerned—it is unpredictable. Treatment of the disease gives results that are often more rewarding, but also often more disappointing, than in most other diseases known to the author.

My interest in the disease originates from work with these children at the clinic for endocrine diseases in Dronning Louise's Children's Hospital, about 10 years ago. The thyroid gland had been a "hidden" organ functionally, whose activity could only be revealed by indirect measurement—oxygen uptake, serum cholesterol determination and by its effect on growth and development, but by this time it was becoming one of those endocrine organs whose function could be determined most directly. The introduction of radioactive iodine into diagnostic procedure, the improved methods of determining iodine in serum and urine, methods for demonstrating the thyrotropic hormone of the pituitary, etc., had naturally an inspiring and fascinating effect on those who were working clinically with these children.

The text-books, for example that of *Wilkins*, 1950, show the position as far as concerned general advances in research on hypothyroidism and knowledge of this condition in childhood. For one thing, it appears that an embryonal defect was regarded as the cause of the majority of "congenital" forms of hypothyroidism. Furthermore, increasing attention was being paid to rare cases of hypothyroidism with congenital goitre, in patients born in regions not lacking in iodine. In such cases, a foetal influence from the mother was regarded as a more likely cause than exogeneous factors. It was considered that the "acquired" juvenile forms of the disease were in most cases the result of an atrophy of rare-

ly recognised causality. Secondary hypothyroidism as a result of pituitary deficiency was still a purely theoretical possibility.

Of the diagnostic methods available, an evaluation of the development of the centres of ossification, particularly conditions in the peripheral epiphyses, together with a record of the growth and development of the child, had been found more useful than determinations of basal metabolism, serum cholesterol and creatine/creatinine excretion.

As for new methods, much was expected of studies with radioactive iodine and determination of protein-bound iodine, but there was no great experience, and the determination of protein-bound iodine in particular was technically difficult.

The aim of the present studies of a group of known hypothyroid children was to arrive at an earlier and more certain diagnosis, as well as to try to differentiate the clinical picture of hypothyroidism into various uniform groups of patients. For this purpose, studies were carried out using radioactive iodine, supplemented by clinical examinations, in the first instance radiological and dental. The author evaluated the roentgenograms personally in all cases, and the dental studies are the outcome of collaboration with Grethe Holst, Dental Surgeon.

The reason for considering it desirable to divide the patients into groups, was the assumption that working with as uniform a patient material as possible would make it possible to emphasize similarities and differences, and these in turn might throw light on new aspects of hypothyroidism. Furthermore, it was thought that the results of treatment could best be evaluated when they could be judged in relation to groups of children with as uniform defects of thyroid function as possible. Finally, there was the consideration that this procedure might contribute to an evaluation of possible hereditary factors.

The grounds for choosing radioactive iodine as a tool were that this technique of investigation seemed very promising to judge from world-wide experience, and that it could be combined with practical work at the hospital, so that the author could carry out all the analyses himself, or with only a little technical help. At this stage, the determination of protein-bound iodine was already being worked-out at central laboratories.

In the present study, I wished to restrict the presentation to the results of the above investigations, for which reason such topics as the anatomy of the thyroid gland and its histology, secondary hypothyroidism, etc., are not included. Likewise, no evaluation has been made of the various recent preparations for treating hypothyroidism. As far as possible the literature has been brought up to about 1958. About 2,500 publications on the subject of hypothyroidism had already been printed by the year 1900. From among this rich material, a special selection was made of such recent studies as discussed conditions in children in particular.

Chapter I.

HISTORY, ETIOLOGY AND MENTAL PROGNOSIS IN HYPOTHYROIDISM

HISTORICAL REVIEW

ENDEMIC CRETINISM

The word "cretin", the origin of which is unknown, first appears in the literature in 1614, and was used by *Felix Platter* in a description of patients living in certain Alpine valleys, and suffering from symptoms corresponding to those still designated by the term *endemic cretinism*. In the course of subsequent centuries, it was pointed out that endemic goitre and endemic cretinism occurred in the same regions.

NON-ENDEMIC CRETINISM

Curling in 1850 described the first cases of absence of thyroid gland, demonstrated at autopsy on two children with the symptoms of "cretinism". He pointed out that it was hardly by chance that the symptoms in these patients with absent thyroid gland resembled the symptoms in endemic cretinism, in which the thyroid gland was enlarged. This line of thought was followed by *C. Hilton Fagge* from Guy's Hospital in London (1871), in his description of what he called "sporadic cretinism", found in children who had never lived in regions of endemic cretinism. *Fagge* believed that in endemic cretinism the goitre represented hypertrophy, in an attempt to compensate for the action of the endemic agency. Should this not succeed, then these patients were in the same position as patients with congenital lack of thyroid gland. In one of the four patients reported by *Fagge*, the symptoms did not occur until eight years of age, following an attack of measles, and it was on the basis of this clinical picture that *Fagge* predicted the symptoms which would presumably develop if the disease occurred in adults.

Gull, in 1874, described two such cases in adult females. *Ord* in 1878 gave an account of autopsy findings, likewise in an adult patient, and introduced the term *myxoedema*, as a result of his demonstration of muciform intercellular masses, which he took to be mucin, and which he conceived as accumulating because the atrophic thyroid gland was unable to excrete it.

In 1884, the Geneva physiologist *Schiff* described deficit signs in dogs following thyroidectomy, although in some cases this also included the effects of parathyroidectomy.

Kocher in 1883 published his results from approximately 100 total thyroidectomies. At that date the opinion still prevailed that the thyroid gland played no part in human physiology. The immediate results of operation were good, but later a "cachexia thyreopriva" developed, with symptoms which we now recognize as those of hypothyroidism in adults and children. In the same year, similar cases were described by the brothers *Reverdin*, who drew attention to the similarity between the symptoms in these patients and in the myxoedematous patients of *Ord* and *Gull*, and—to a minor degree—the symptoms in patients with endemic cretinism.

Around 1890, it was recognized in England that myxoedema and cachexia thyreopriva were identical, and that cretinism was myxoedema in children.

In a series of 60 "cretins" from the USA and Canada, *Osler* in 1893 described a number of patients with goitre and hypothyroidism, who came from districts where there was no endemic cretinism. *Osler* also noticed that among these "non-endemic goitrous cretins" there were a number of cases among siblings. According to the literature, this type of patient occurs rather rarely, but in recent years the type has had great significance for an understanding of important aspects of hormone production in the thyroid gland under normal and pathological conditions.

Once the significance of the thyroid gland was established, the way was open for therapy. At first this consisted of attempts at implantation. A number of these were successful, in so far as the patients became symptom-free for a short period. This effect did not depend on the independent functioning of the transplant, but—which was also recognized—on the effect of absorption of the implanted thyroid tissue. Experiments soon followed with injection and oral ingestion of thyroid extracts from various animals, and later on treatment with desiccated thyroid tissue. *Howitz* (1892) and *Vermehren* (1893) were the first to introduce such treatment in Denmark.

It is interesting, and very informative, to see how near some of these earlier investigators of hypothyroidism come to the present-day picture of the various forms of this disease. *Wieland*, for example, in 1912 gave a description of the "hypothyroid constitution", in *Zeitschrift für Kinderhkl.*, which even today appears to be valid on practically all points. The same issue of the journal contained an energetic discussion as to whether "cretins" in Switzerland are the descendants of Neanderthal man! *Wieland* begins by advocating an even older suggestion (*Lanz* and *Hertoghe*) for the introduction of the term "hypothyrosis and athyrosis". This suggestion occurs repeatedly in the literature—see for example the introduction to the present study—but it appears as if the non-characteristic designations which came into use early on have a great

sticking power. At some future date, workers may possibly reach agreement on a common designation after a tiresome search through the literature of the subject under 5-6 different designations, and it seems to the present author that the terms given above will be recognized as the clearest and most characteristic. In *Wieland's* view, based on his own clinical experience and autopsy findings and those of other authors, most of these children have a congenital, more or less complete absence of thyroid gland as a result of a *vitium primae formationis*. The degree of severity of the clinical picture and the time of onset of the disease after birth depend on the amount of thyroid tissue found in the new-born infant. Hypothyroidism in children as a result of post-natal thyroiditis, or the like, is only of rare occurrence. Those cases which apparently become manifest following an infection, are merely triggered-off by it; the infection is not their causal factor.

Wieland quotes previous reports of autopsy findings of hypoplasia and partial aplasia of the thyroid gland, and mentions the possibility that ectopic, sublingual "thyroid anlage"—observed for example by *Seldowitsch*, *Chamisso* and *Ungerma*n—can "deputize" for a normally sited thyroid gland. *Wieland* stresses that there are only a limited number of autopsies to confirm the correctness of the point of view presented, that the conclusion must be based on the clinical observations of individual observers, and that there is no definite opinion on how much or how little active thyroid tissue is necessary for the maintenance of normal function. In addition, the article contains reports on how the time of onset of the disease can be estimated with the aid of bone development, determined from roentgenograms.

In many quarters, these points of view do not seem to have gained the acceptance they deserve, possibly because as mentioned they are based on autopsy findings in particular, and these are rarely available. For some time, it was the general opinion that the congenital cases of "myxoedema" were the result of lack of thyroid tissue, and that most of the acquired forms were the result of atrophy of unknown cause. In addition, a few were considered the sequelae of thyroiditis, partial strumectomy, etc. (see for example *Wilkins* (1950)).

It was not until the introduction of radio-active iodine in diagnostic procedure that a far broader picture was obtained of the mutual relationships between the various clinical forms of the disease and the amount and nature of the thyroid tissue present.

The theory that "congenital dysgenesis" of the thyroid gland was also the cause of some of the clinical pictures of later manifestation was hereby "re-discovered".

THE ETIOLOGY OF HYPOTHYROIDISM IN CHILDREN

The reason for congenital absence of thyroid gland is still unknown. One of Fagge's contemporaries believed that it was the result of drunkenness in one or both parents at the moment of conception. This, as well as most of the other points in the etiology of the disease, remains unelucidated. The influence of hereditary factors will be discussed later.

Very little is known on the significance of intrauterine infections for thyroid aplasia. The author, in 1954, was the first to describe a case of congenital toxoplasmosis in a three-month-old child in whom no trace of thyroid tissue—either normal or ectopic—could be demonstrated post mortem after careful histological studies. Similar cases have been described by *Aagaard* and *Melchior* (1959). Whether these isolated cases are merely chance coincidence—toxoplasmosis is not uncommon in Denmark—or whether there is another association, could not be established. In a further two patients in the present material (Cases no. 2 and 45) a positive toxoplasmosis reaction was found in mother and infant, and the question of a possible causal relation will be discussed.

Hubble (1956) has ventilated an interesting possibility: that the lack of thyroid tissue in the newborn may in some cases be the result of an absence of stimulation of the thyroid gland by the foetal pituitary (lack of foetal thyroid stimulating hormone (TSH)). The fact that, in other cases, the pituitary is strongly active in athyrotic patients is shown in the same study, in which the autopsy report is given of a three-month-old infant in whom a quite small thyroid remnant was found together with signs of thyrotropin-stimulation and pituitary showing signs of strong activity histologically.

In the study by *Andersen* (1954) mentioned earlier, increased TSH-activity was demonstrated in the serum and the skin, in spite of the pituitary showing signs of toxoplasmotic infection, the child at that time being totally athyrotic. It is obviously impossible to arrive at any precise conclusions on the size and activity of the thyroid gland in this infant *in utero*, but absence of centres of ossification around the knee in the third month of life showed that there must have been hypothyroidism before birth (see later).

On the whole, therefore, it must be said that we still do not know the reason for either the complete athyrotic condition or for the other forms of hypothyroidism. An exception to this, however, appears to be certain forms of hypothyroidism with goitre, the result of a genetically determined enzyme defect, which will be mentioned in further detail in the section on hypothyroidism with goitre.

THE MENTAL PROGNOSIS FOR CHILDREN WITH HYPOTHYROIDISM

Mental retardation has been recognized as a sign of hypothyroidism as long as the disease has been known. Likewise, it is a wellknown fact that the effect of treatment on the development of the intelligence is far more uncertain and capricious than its effect on somatic development. Views still vary on the cause of this, perhaps the most important of all aspects of hypothyroidism.

As early as the beginning of the century, there were reports on the absence of effect of hormone therapy on mental development. *Wieland* (1912) and *Tredgold* (1916) state that even though treatment earlier than the age of three months resulted in complete cure in certain cases, this was so only rarely when the patients were not treated until after the age of one year, even though improvement usually appeared. *Tredgold* (1929) later assumed that there were possibly two types of the disease. In the one type, the mental defect is the result of hypothyroidism and these children become normal on treatment. In the other type, in addition to their hypothyroidism, the children also suffer from a *primary mental defect*, which does not improve on treatment. *Lazar & Nobel* (1924), on the basis of six cases followed for some time by means of various developmental tests, maintained that the intellectual development depends directly on the time of institution of treatment and on its intensity. *Gesell et al.* (1936), likewise on the basis of six cases, came to the conclusion that the final result did not depend so much on the age and degree of maturity of the patient at the commencement of the treatment, as on the "physiological capacity and latent power of growth in the neuro-endocrine system". They found in addition a close association between the behaviour of the child and its mental development, and stressed the prognostic value of behaviour-pattern studies. *Aldrich* (1936) is the spokesman for treatment with "subtoxic" doses, being unfavourably impressed by the many poor results, and on the grounds that the various tissues may have varying requirements for thyroxine, so that treatment which may normalize somatic growth and development need not be adequate for an optimum course of mental development. *Lewis* (1937), in a material totalling 79 cases in the age group 3-58 years, found a fairly rough correlation between age at commencement of treatment and the final level of intelligence. *Wilkins* (1938), who has extensive personal experience with hypothyroid children, stresses the significance of a vigorous and persistent therapy from the very start, among other reasons because the child's nervous system may suffer damage already during the intrauterine period, or in early childhood. Further, he stresses the value of carefully determining the age of bone development and other somatic and mental development at the commencement of treatment, as a guide to the

effect of the therapy. *Brown et al.* (1939) stress that early diagnosis and vigorous and persistent treatment are decisive for a good mental prognosis. *Goodkind & Higgins* (1941) do not consider that age at commencement of treatment plays any decisive part, as six of their patients receiving treatment before the age of one year remained severely retarded.

Bruch & McCune (1944), in a material of 23 patients, found that the development prior to treatment was a guidance for evaluating the prognosis. They found only poor agreement between adequate treatment begun early and the final stage of intelligence in the children, and they believed that in certain cases the cerebrum and thyroid gland could be damaged simultaneously. They found no support for considering that hypothyroidism in the mother should be a factor of significance, but on the contrary they point to the fact that undernourishment of the mother might have some significance. Furthermore, they warned against the use of high dosing in all cases, as such high doses could overshoot the mark, resulting in irritable, poorly adjusted children, and directly inhibiting the development in certain cases.

There are not many cases in which the actual nature of the cerebral damage has been investigated in patients with hypothyroidism, but *Whipham* (1885), *Marinesco* (1924) and *Lotmar* (1929) have demonstrated vascular changes, signs of arrested development and defects of maturation, to mention some features. It is difficult to decide how many of these changes are present at birth, and which are the result of a later development. Animal experiments with thyroidectomy in new-born rhesus monkeys (*Pickering et al.* 1953) showed delayed development and defects of maturation in the neurones, for example, and they were able to demonstrate subsequently that this could be hindered by administering sodium l-thyroxine to a corresponding group of animals. In the cases mentioned, the athyrotic condition was produced post partum. *Barnett* (1948) demonstrated corresponding changes in rats whose mothers were treated with thiouracil during pregnancy.

Ross and Schwab (1939) demonstrated electroencephalographic changes in children with hypothyroidism. Generally, they found a slow α -rhythm of low frequency, which became normalized after treatment.

In Sweden, *d'Avignon & Melin* (1949) demonstrated that patients who had improved mentally as a result of the treatment had a normal EEG, while pathological curves were obtained in unimproved cases. *Topper* (1951) found similar conditions.

Numerous studies have been made on the same lines as those quoted above, which show the dominant points of view.

In Scandinavia, major studies of the mental prognosis for hypothyroidism in children have been submitted by *Marvel* (1939), for example. In a collected Norwegian material of 16 patients, observed for a period of 6-32 years, only one patient was found with an I. Q. > 80, and no relationship was found

between the time of commencement of the treatment and the final somatic and mental development.

In Denmark, *Gørtz & Rothe-Meyer* (1943) have given an account of 25 patients treated during the period 1907–1940, the majority at Dronning Louise's Children's Hospital. Twenty-four of these were followed up. Four of them had intelligence quotients between 90–100, while the remainder had lower values, many of them very low. These authors advocate the importance of an early and effective treatment.

D'Avignon (1958) reaches the same conclusions for his Swedish material of 118 patients selected from a group of 300 patients in various parts of Sweden throughout the last 50 years, diagnosed as having hypothyroidism.

Most major series presenting the results of treatment suffer from the fundamental weakness that the material is very inhomogeneous, particularly as far as the earliest, most important period is concerned. From the start, the children are diagnosed and treated in a number of different places, according to criteria which are far from uniform, and the information as to treatment, etc., during the first years often becomes exceedingly faulty in the course of time. The reason for this is that the disease is relatively uncommon, and that it was not until recently that these patients were collected in special clinics, so that one individual or group could study them thoroughly and prepare a sufficiently uniform material for evaluation.

As an example of this might be mentioned the report by *Smith, Blizzard & Wilkins* (1957) on the mental prognosis of 128 children observed in the same clinic throughout the period 1935–55. The period of observation varied from 1–10 years prior to the intelligence determination. In the majority of cases this was based on I. Q. tests, and in 19 cases on clinical evaluation. The material was divided into three groups according to an estimate of the degree of severity of the symptoms, supplemented in some cases by radioactive iodine tests, etc.

Treatment was carried out with a dessicated preparation of thyroid gland and considered adequate provided it "promptly and permanently caused the symptoms to disappear and ensured normal body-growth and bone development, and had reached full strength within two months of commencement".

Smith et al. concluded that adequate treatment instituted early was of decisive significance for the mental prognosis and to counteract neurological disturbances in congenital hypothyroidism which gave early symptoms and—though to a less pronounced degree—in the cases of later manifestation.

Chapter II

UPTAKE OF I^{131} IN THE THYROID GLAND OF EUTHYROID CHILDREN

This chapter describes measurements of the uptake of radioactive iodine by the thyroid gland, together with the results of such determinations in euthyroid patients.

The basis of the application of radioactive isotopes of iodine to studies of the function of the thyroid gland, is that these substances, in amounts whose radioactivity does not seem to affect the properties of the cell, can be treated chemically and physically just like stable iodine. The radioactivity makes it possible to "trace" the path of the iodine and its fate in the organism.

Hertz et al. in 1938 showed that the iodine isotope I^{128} (half life of 26 minutes) was taken up rapidly and selectively in the thyroid gland of the rat. The application of isotopes of iodine in patients with various thyroid diseases followed rapidly (*Hamilton & Soley* 1939). In this case, I^{131} was used, with a half life of eight days, and this is still the iodine isotope most used for direct measurements over the thyroid gland and for determining the iodine excretion in urine and faeces.

During the past twenty years, innumerable studies have been made along these lines. Those of *Skanse* (1949), *Blom* (1954) and *Larsson* (1955) might be mentioned among major studies, with detailed examination of the various basic factors in the technique and analysis, and giving the literature on the subject.

AUTHOR'S TECHNIQUE OF INVESTIGATION

The technique of investigation used in the present study does not differ in principle from that employed in former studies of this nature. When, in 1954, it was decided to use isotopes for diagnoses etc. of children with thyroid disease, two points in particular received attention: 1) employment of the minimum doses possible, and 2) employment of a technique which was simple enough to be fitted into the daily clinical work.

Carrier-free radioactive iodine (I^{131}) is used in the following dosages: 0.25 micro-Curie (μC) for infants of 2-3 months, approximately 0.5 μC for

larger infants and small children, and 1–1.5 μC for older children. In a few cases, 2–3 μC was given to 16–17-year-olds, when the method was being introduced. These doses were far lower than the ones previously used for the same purpose, and there is still no one working with lower doses (see later). It may be added for comparison that the doses of I^{131} , set down in 1959 by the "International Committee for Radiation Protection" as the maximum permissible for *healthy* children in the case of accidental peroral consumption, are of the same order of magnitude, although somewhat greater.

The maximum amount of I^{131} recommended by the United States Atomic Energy Commission for routine tests on *adults* is 50 μC . With this dose, a thyroid gland weighing 20 g will receive an ionizing radiation of 131 rad, with a 40 per cent uptake and complete physical degeneration. Under the same conditions, a thyroid gland in an infant will receive approximately 7 rad as the result of a dose of 0.25 μC . The normal dose of 0.25 μC given to an infant whose thyroid gland weighs 2 g would correspond to 2.5 μC in an adult with a thyroid gland weighing 20 g. An adult dose of this value is less than the dose used, at any rate until recently, by most workers.

The apparatus is chosen with an eye to high sensitivity for the measurement of γ -rays.

A "Tracerlab"—P. 20 QG scintillation detector is used with a crystal diameter of 1". This crystal picks up about 2,500 impulses—counts per minute—(C. p. M.) from 1 μC I^{131} at a distance of 15 cm, with a background radiation of about 850 CpM in the unscreened condition. For recording the impulses captured, the detector is connected with a "Tracerlab" S. C.-33—"1,000" Scaler equipped with a stop-watch, which automatically cuts off the counting after a preset time, which can be varied within a period of one hour in 5.0 sec. intervals.

To reduce background radiation and the direct or reflected radiation ("scattering") from the tissue around the thyroid gland, the detector is surrounded by a lead shield. In this way the crystal is covered throughout by a lead cone, approximately 8 cm thick, with the exception of the front. The radiation reaches the crystal through a slightly conical channel, approximately 8 cm deep, with an external diameter of about 2½ cm. At the bottom of the channel, immediately in front of the crystal, a 2 mm thick lead plate is placed. In this way the background radiation is reduced from about 850 CpM to about 110 CpM. The detector + lead shield are suspended, freely moveable, above the head of the couch on which the patient is being examined.

The measurements are carried out with the child lying supine, a small round cushion being placed under the neck. It was necessary to immobilize smaller children in various ways, but in general there were no great difficulties in concentrating the attention of the children up towards the apparatus, so that they remained quiet during the period of the experiment.

The distance was adjusted with the help of a metal chain fastened to a plug fitting into the opening of the lead shield. With the counter placed vertically, and the chain just touching the neck of the child over the site of the thyroid gland, the distance between crystal and skin is 20 cm. This method of measurement does not frighten a child nearly so much as the use of polished, possibly sharp measuring pins, etc., and may presumably be considered precise enough for the purpose, when one considers, for example, that the precise distance between the skin and thyroid gland cannot be determined. The measurement is usually continued for 10 minutes.

In a number of cases, particularly in infants, who are difficult to keep still, the detector is placed directly on the child's skin over the thyroid gland, without the lead shield, which is too awkward for this purpose. The same technique is used in localizing any retained, sublingual thyroid tissue, first measuring directly towards the thyroid gland and then turning the detector in such a way that it points up towards the foramen coecum linguae.

In such cases, this method of measurement gives a better geometry than measurements carried out at a distance of 20 cm on two areas which, in small children, are so closely adjacent. In a similar manner, the region inferior to the thyroid gland and over the mediastinum is searched for ectopic thyroid tissue.

From the beginning of 1955, when the first patient was found in whom the sole site of uptake of I^{131} was in the sublingually-retained thyroid tissue, all patients showing no or slight activity of the thyroid gland at its normal site have been regularly examined for ectopic activity.

CALCULATION OF THE ACTIVITY IN THE THYROID GLAND

At first, the amount of I^{131} administered was measured at a distance of 20 cm immediately prior to giving the dose, and the activity over the thyroid gland was thereafter measured at intervals of hours or days, at a distance of 20 cm. The values found, corrected to the time of commencement for physical degeneration (50 per cent in eight days), were expressed in percentages of the activity administered.

However, another technique was soon chosen, which has been used unchanged since. Before commencing the test, two equal amounts (about 10 ml) of I^{131} are measured out with a pipette. The patient drinks the one sample or is given it by tube, then the container is rinsed twice with water which the patient also drinks. The other sample is stored in an ordinary "blood sugar test-tube" (2.5. x 10 cm cylinder) and measured during the corresponding period immediately before or after each measurement carried out on the patient, and at the same distance from the detector. The activity over the

thyroid of the patient is then expressed as a percentage of the activity of the sample. In this way, a correction for physical degeneration is avoided and the results are independent of any possible changes in the sensitivity of the counter. The results following the two procedures showed no difference.

Repeated measurements were carried out at various times on almost all patients. At first, measurements were made at intervals of a few hours varying to a few days, later after about 24 and 48 hours as a rule. In special circumstances, as for example in a hypothyroid patient with goitre, where sudden changes in uptake could be expected within a short period of time, frequent measurements were made at the beginning of the test until the course of the curve could be estimated.

The statistical uncertainty in recording the impulses is about 2 per cent, as on the average about 8,000 ~~CpM~~ are recorded. The limits varied between about 1,000 and 20,000 ~~CpM~~. The order of magnitude of the deviations be-

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deposition of radioactive iodine perivascularly for a shorter or longer period of time.

The urine was examined for radioactivity in only a few cases. The drawbacks and inaccuracies of collecting the urine quantitatively from infants and small children—and for that matter also from older children not in bed all day—are great, and as it was the amount and site of the active thyroid tissue that was of interest, and as measurements of urine were not particularly useful in this connection, such measurements were omitted.

In calculating the results, allowance has not been made for the quantity of I^{131} left in the tube after rinsing twice. According to measurement this amounts to only 1–2 per cent of the dose given. Likewise, attention has not been paid to scattering from the tissues outside the thyroid. Phantom experiments, using water as a background to imitate the tissue around the thyroid gland, showed that the result was very little influenced by these parts, < 5 per cent. Furthermore, the errors discussed will influence the final result in opposite directions.

A considerable number of methods have been reported in the course of

time to correct for scattering: measurements on various phantoms, measurements over the neck of the patients after lead screening of the thyroid gland, etc. Others, for example *Blom*, deduct a fixed value—7 per cent for children—from the results. We found that the use of phantoms, watercontainers of varying size according to the age of the children, etc., was inconvenient and time consuming. Further, the correction obtained in this manner appeared to be insignificant compared with the spread of the results and with the difference between euthyroid and hypothyroid patients, so we soon omitted the correction. *Orvis et al.* (1957) are also of the opinion that the correction for scattering is generally insignificant in routine measurements, particularly after a lapse of 24 hours.

THE IODINE UPTAKE IN THE THYROID GLAND OF EUTHYROID CHILDREN

PREVIOUS STUDIES

Hamilton et al. (1943) made the fundamental observations of the uptake of I^{131} in the thyroid gland of children. These observations were subsequently confirmed by numerous other workers. Previous findings in euthyroid children will be reviewed in what follows. The results of the investigation of children with thyroid disease will be discussed in the subsequent chapters. As the review shows (table I), the uptake in the thyroid gland after taking I^{131} lies around 20–50 %. There is undoubtedly a very considerable biological scatter, and the materials are not completely comparable. As a result of improved methods of investigation and the employment of radioactive iodine without or with only minimal amounts of stable iodine as a “carrier”, recent investigations give a higher uptake than earlier, as was already pointed out by *Hamilton*. On the whole, the results correspond to what is found in euthyroid adults (*Skanse, Larsson*).

Iodine uptake in the newborn

Some uncertainty appears to exist on one point, the *conditions in young babies*. *Van Middlesworth et al.* (1954) found greatly increased values (61–97 %) in five out of six newborn, 2–3 days old babies. In the sixth baby the uptake was 46 %. *Martmer et al.* (1956) found values of 20–30 % after 24 hours in 65 prematures and five full-term infants aged 2–63 days, many however only a few days old. There was a scatter in the values of 10–60 %. *Sheline et al.* (1957), in a material of 20 children aged 12 days to 17 years, found no increase in the uptake, in the case of the infants. *Brante et al.* (1956), report a considerable scatter in the values in prematures. *Gomirato-Sandrucci & Nicola* (1958) found an uptake of 59.3 % in premature infants

aged 2-9 days (8 patients), 46.5 % in premature infants aged 16-26 days (7 patients), and 40.8 % in premature infants aged 32-65 days (9 patients). The uptake was measured after 24 hours, and the highest values (90 %) were found during the first 2-3 days. The scatter was very great.

Tangheroni et al. (1958) found 71.1 ± 17.2 % in 12 breast-fed infants aged six months or less and 42.2 ± 10.4 % in bottle-fed infants in the same age group. Ten infants in their second half-year had an uptake of 40.8 ± 12.1 %. Very high values, 90 %, were found in the youngest breast-fed children (10-13 days old) in this material. The difference between breast-fed and bottle-fed children is remarkable. The difference in the material discussed might result from the age distribution being different in the two groups, as there were six infants under one month in the breast-fed group, while there was only one infant under one month in the other group, and as mentioned the high values are found during the first month.

The large scatter in the measurements in premature infants may well be an expression of variations in the degree of maturation, together with other individual variations. A further factor which might play a role in this connection is the consumption of cod liver oil and other vitamin supplements, whose iodine content might inhibit the function of the thyroid gland. *Oliner* (1957) mentions cod liver oil as one of the causes of low uptake of I^{131} in children. This may well play a part, particularly in the above category of children, as custom and practice vary with respect to the type, amount and time of commencement of vitamin supplement to breast-fed infants, bottle-fed infants and premature infants.

In addition, as iodine reaches the infant in the milk, the diet and vitamin supplement enjoyed by the mother (or the cow) may also be significant for the thyroid function of the infant.

From what has been said above, however, it seems that in some children, at least, the thyroid gland takes up iodine very actively during the first few days of life. The values of protein-bound iodine are higher in the immediate post-natal period than later (*Danowski* 1951, *Man* 1952). It is still not clear whether this involves a true hyperfunction, a shift in the fluid distribution in the body, or a reaction to increased peripheral consumption (e. g. *Oliner* 1957).

Apart from the conditions in the newborn as mentioned above, most of the series show no variation in uptake according to age, sex or dosage. Exceptions are those of *Gali* (1956) and *Brante et al.* (1956), who find increased uptake in girls before and during puberty.

Table I.
Previous investigations of iodine¹³¹ uptake over the thyroid in euthyroid patients.

Author	Year	No. of pts.	Age	Dosage in μC	Percentage uptake
Hamilton et al.	1943	3	4 yr.-10 yr.	14 mg. iodine	2% after 5 days
Quimby & McCune	1947	32	1 yr.-14 yr.	20-40	$12\% \pm 3.6$ after 48 hrs.
Lowrey et al.	1949	12	1 mth.-14 yr.	20-50	400-1000% after 24 hrs., of the initial activity over the thyroid gland.
Reilly & Bayer.	1952	25	9 mths.-15 yr.	$< 6 \text{ yr.}-5$ $> 6 \text{ yr.}-10$	16% (8.7-29.8%) between 24-96 hrs.
Pickering & Miller	1953	5	1 yr.-10 yr.	15-40	$12\%-20\%$ after 24 hrs.
Silverman & Wilkins	1953	20		1 per kg i. v.	Activity over the thyroid gland minus activity over the femur after 24 hrs. (18-176 counts per second).
Horst & v. Harnack.	1953	25		5-40	46% (15-60%) after 24 hrs. 52% (15-60%) after 48 hrs.
Bernheim et al.	1954			$< 10 \text{ yr.}-20$ $> 10 \text{ yr.}-50$	approx. 20% after 24 hrs.
van Middlesworth.	1954	7	newborn, 2-3 days old	1 per kg	61-97% (6 patients) after 24 hrs. 46% (1 patient)
Jaimet et al.	1955	15	5 yr.-9 yr.	50	31% (10-50%)
Friedman.	1955	68	$1\frac{1}{2}$ yr.-16 yr.	10-20	$21.3\% \pm 6.7$ (9-38%)

Table 1 contd.
Previous investigations of iodine¹³¹ uptake over the thyroid in euthyroid patients.

Author	Year	No. of pts.	Age	Dosage in μC	Percentage uptake
Gali et al.....	1956	45	4 yr.-15 yr.	25-50	38-64%
Martner et al.....	1956	65	premature, 2 days-2 mths.	5	25% (10-60%)
Brante et al.....	1956	97	premature-15 yr.	1 per 7 kg $\frac{1}{2}$ - $\frac{1}{4}$ of this dose given to infants	approx. 37% mean value. Higher up- take in girls at puberty. Wider range for premature infants
Tubiana & Ravaud.....	1956	62	2 yr.-16 yr.	10	43.24% (40-47%)
Oliner et al.....	1957	60	2½ mth.-18 yr.	< 10 yr.-25 > 10 yr.-50	31.7% \pm 7.63%
Della Maggiore & Pordelli ...	1957	30	6 yr.-10 yr.	1 per kg	53% \pm 11.8%
Sheline et al.....	1957	44	12 days-17 yr.	?	22.1% (12-4.5%)
Tangheroni et al.....	1958	32	10 days-12 mths.	1 per kg	Breastfed babies \leq 6 mth.: 70.1% \pm 17.2% after 24 hrs. Bottle-fed babies \leq 6 mth.: 42.2% \pm 10.2% after 24 hrs. 10 children 6-12 mths.: 40.8% \pm 17.1% after 24 hrs.
Gomirato-Sandrucci & Nicola.	1958	24	premature, 2 days-65 days	1 per kg	55.25% (34-93%)

AUTHOR'S STUDIES

An actual "normal material" has not been examined. All cases examined have been suspected of suffering from thyroid disease. A group of these cases has been identified as euthyroid, on the basis of other tests and their subsequent course. For several reasons, a control group of cases such as these—resembling children with thyroid disease in a number of ways, several having also received thyroid treatment for a shorter or longer period of time—is preferable to "completely normal children" as a control material.

The euthyroid comparison group comprises 44 patients, one of whom was examined twice. The I^{131} uptake in the thyroid gland of these children was determined a total of 124 times, and the results are recorded in table II.

The patients are distributed according to sex and age as follows:—

	Girls	Boys
≤ 1 year	1	1
1– 5 years	4	3
5–10 years	9	6
> 10 years	10	10
total	24	20

The fact that the majority are in the older groups is associated with the manner of obtaining the material. In these age groups it was more difficult to distinguish the patients from those with the late, insidious forms of hypothyroidism. No correlation has been found between the percentage uptake and the dose of I^{131} given, nor was this anticipated, as the radioactivity is associated with iodine amounts insignificant in relation to the daily intake of iodine. Nor was any association found between the activity demonstrated and the height and weight of the children. The influence of age on uptake will be discussed later.

Among the euthyroid patients examined, four were not included in the above group: case records no. 126/55, 52/56, 468/57 and 1269/57. In these patients, an exact evaluation was made impossible on account of slight vomiting or regurgitation, severe excitability and resistance to the examination. However, the results showed that there was active thyroid tissue in satisfactory amounts.

In addition, 7 euthyroid patients were examined who were under thyroid treatment (cases no. 144–150). The first few of these patients were examined to decide whether it was necessary to withdraw the thyroid treatment prior to the investigations. Reports on this point were contradictory at the time. The remainder of the patients were a number who "had not recalled" having had thyroxine treatment in the period before the examination, but recalled this later.

These patients are recorded in table III which, compared with table II, shows the inhibiting influence of thyroxine on the normal thyroid gland.

Table II.

Euthyroid patients—control group.

Cases no. 100-110.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
100	1483/54	M	9 ¹ / ₁₂ yr.	suspected neurosis, hyperthy.	0	7	14	30	32		30	
101	288/55	F	4 ⁹ / ₁₂ yr.	not found	0	23	20	36				
102	132/55	F	11 ¹⁰ / ₁₂ yr.	obesity,	0	19		32	41		38	
103	137/55	M	12 ¹¹ / ₁₂ yr.	oligophrenia	discont.	12	24	38	38	42	42	190 hrs.;
104	141/55	F	11 yr.	oligophrenia	1 ¹ / ₂ mth.	0		62	40	61	60	40
105	225/55	M	11 ⁴ / ₁₂ yr.	obesity, dwarfism,	0	29	32	58	54	55		212 hrs.;
106	85/55	F	8 yr.	constip. mental	0	7		62	61	60	51	39
107	822/55	M	9 ⁷ / ₁₂ yr.	retard'n	discont. 6 mths.		25	34	25			
108	351/55	M	12 ⁷ / ₁₂ yr.	obesity	0			60	60	58	55	
109	973/55	M	10 yr.	dwarfism, obesity	0			34	36	39	40	
110	307/55	F	11 ¹¹ / ₁₂ yr.	malrotation of duodenum, obesity, dwarfism, mental retard'n.	0			37	43	42		

Table II contd.
Euthyroid patients—control group.
Cases no. 111-119.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	Percentage uptake of iodine ¹³¹ over the thyroid gland after:						
						0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
111	579/55	F	7 ¹¹ / ₁₂ yr.	obesity, dwarfism, mental retard'n ?	discont. 9 mths.			46	41			
112	716/55	F	10 yr.	obesity, mental retard'n ?	discont. 2 mths.		44		44-45			
113	747/55	F	15 ⁹ / ₁₂ yr.	obesity, mental retard'n.	discont. 2 mths.		39	46				
114	1300/55	F	14 ⁹ / ₁₂ yr.	dwarfism, mental retard'n.	0		47		44			
115	102/56	F	7 ¹¹ / ₁₂ yr.	retard'n. obesity, mental retard'n.	0		46	43				
116	27/56	F	9 ² / ₁₂ yr.	obesity, elevated serum chol.	0		45	35				
117	206/56	M	13 yr.	obesity, mental retard'n. constip.	0		44	44				
118	233/56	M	10 ⁴ / ₁₂ yr.	dwarfism, obesity	0		42	46				
119	205/56	F	13 ⁹ / ₁₂ yr.	mental retard'n, dwarfism	discont. 1 mth.		58	62				

Table II *contd.*
Euthyroid patients—control group.
Cases no. 120-127.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
120	810/56	M	16 ⁵ / ₁₂ yr.	obesity, dwarfism, sequelae of skull fracture	0			34				
121	454/56	M	2 ³ / ₁₂ yr.	epicanthus, mental retard'n.	discont. 5 mths.			37				
122	1062/56	F	4 ⁵ / ₁₂ yr.	encephalopathy	discont. 5 weeks		26	39-40				
123	1143/56	M	9 ⁸ / ₁₂ yr.	cerebral paresis, mental retard'n.	0		44	50				
124	1245/56	F	15 yr.	encephalopathy, mental retard'n.	0		47	45	44		45	
125	1475/56	F	9 ¹ / ₂ yr.	dwarfism, obesity	0		53	50				
126	1560/56	M	2 ¹¹ / ₁₂ yr.	atypical mongolism	0		40	50		35		
127	135/57	M	8 ⁷ / ₁₂ yr.	macroglossia, retarded bone development	0		40			40		

Table II contd.
 Euthyroid patients—control group.
 Cases no. 128-135.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
128	433/57	F	1 ¹ / ₁₂ yr.	phys. and mental retard'n. from 6 mths.	0			50	50			
129	479/57	M	1 ⁵ / ₁₂ yr.	constip., phys. and mental retard'n.	0			37				
130	566/57	M	12 ¹ / ₂ yr.	encephalopathy, mental retard'n.	0			40	34			
131	450/57	F	14 ² / ₁₂ yr.	dwarfism obesity, constip.	0		30		27			
132	708/57	M	12 yrs.	dwarfism, constip., Brother has ect. thyroid tissue	0		47		40			
133	654/57	F	3 ¹⁰ / ₁₂ yrs.	constip., dwarfism	0		46		37			
134	784/57	F	15 ³ / ₁₂ yr.	obesity, constip., amenorrhoea	0			51-50				
135	1168/57	F	9 ¹⁰ / ₁₂ yr.	mental retard'n., excessive obesity	discont. 4 mths.			68	66			

Table II contd.
Euthyroid patients—control group.
Cases no. 136-143.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	Percentage uptake of iodine ¹³¹ over the thyroid gland after:						
						0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
136	1459/57	M	14 yr.	obesity mental retard'n. dwarfism, retarded bone development, various mal- formations	discont. 3 1/2 mths.		38		40			
137	38/58	M	9 1/2 yr.		0			30	30	34		
138	431/58	F	8 3/12 yr.	dwarfism	0					59		
139	44/58	F	8 1/12 yr.	hypertel- orism, atrophia	discont. 3 mths.			55 31				
140	620/58	F	8 7/12 yr.	phys. and mental retard'n. mongolism	0		56					
141	925/58	M	10 1/12 yr.		discont. 1 yr.		41					
142	1070/58	M	14 yr.	mental retard'n., obesity dwarfism, constip. encephalo- pathy, mental retard'n.	0		45	46	49			
143	196/59	F	10 7/12 yr.		0		44	42	45			
130	163/59	M	14 1/12 yr.		0		38-33					

Table III.
Euthyroid patients—control group. Examined during thyroid treatment.
Cases no. 144–150.

Case no.	Case record no.	Sex	Age at exam.	Diagnosis	Thyroid treatment	Percentage uptake of iodine ¹³¹ over the thyroid gland						
						0 hr.	12 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
144	288/55	F	5 yr.	obesity	300 u./day for 2½ mth.	5		4				
145	384/55	F	9½ yr.	obesity	200 u./day for 2½ mth.		8–10	8–9	9	9	11	
146	516/56	M	14½ yr.	obesity, hypothyroidism not found	200 u./day for 3 yr.		22				22	
147	606/56	F	19 yr.	obesity	200 u./day for ½ yr. Later, thy. prep. of unknown strength		approx. 1	1	3	3		
148	278/57	M	8½ yr.	obesity, constip.	100 u./day		15	13				
149	492/57	M	9½ yr.	atypical mongolism	200 u./day for several years			0				
150	1410/57	F	15½ yr.	obesity, dwarfism	100 u./day for 8 days		9					

CALCULATION OF THE MEAN AND THE STANDARD DEVIATION FOR THE CONTROL GROUP

At first, the uptake percentages for the individual patients show a steep increase, then reach an approximately steady level after about 24 hours. In the 43 patients, a mean value of $M = 43.5 \pm 1.5$ is found after 24 hours, and after 48 hours the value found for 37 patients is $M = 45.2 \pm 1.5$. In those cases where the values were not measured after exactly 24 and 48 hours, the values for the individual patients were found by interpolation on the individual curves. As an estimate of the spread in the groups, a value of $S = 9.7$ was found for the standard deviation.

In 35 patients, measurements are available for both 24 hours and 48 hours. By taking the difference between the two times for the individual patients, it is found that the uptake percentage after 48 hours is on an average 0.89 ± 0.84 times greater than the uptake percentage after 24 hours. This difference is not significant, as we find $t = 1.06$ (t is equal to the difference of the means divided by the estimate of the standard error of the difference. $t = 1$ corresponds to the 30 % limit, $t = 2$ corresponds to the 5 % limit). For the group as a whole, therefore, no significant change in uptake percentage can be demonstrated in the course of the second 24 hours.

Considering the girls aged 10–14 years, it is found that for this group, there are 11 girls with a mean uptake percentage after 24 hours of $M = 46.1 \pm 5.7$. The remaining 32 patients have a mean uptake percentage of 42.6 ± 1.6 . The difference is not significant, as $t = 0.87$.

After 48 hours, a mean uptake percentage of $M = 47.8 \pm 3.1$ is found for 12 girls aged 10–14 years, and for the remaining patients $M = 43.9 \pm 1.6$. The difference is not significant here either, as $t = 1.11$.

Fig. 1 shows all the measurements of the euthyroid patients (cases no. 100–143), together with the mean and the standard deviation, as mentioned above. The mean value after a period of 24 hours lies somewhat higher than found, for example, by Larsson (1955) in an adult Swedish material, 37.5 %, but lower than found in a recently published study of Danish euthyroid adults (Friis & Korsgaard Christensen 1959): 54.6 %. Biancalana *et al.* (1957) report a mean uptake for euthyroid adults after 24 hours of 40.1 ± 14.2 (24–73.5 %). These differences may be the result of varying techniques.

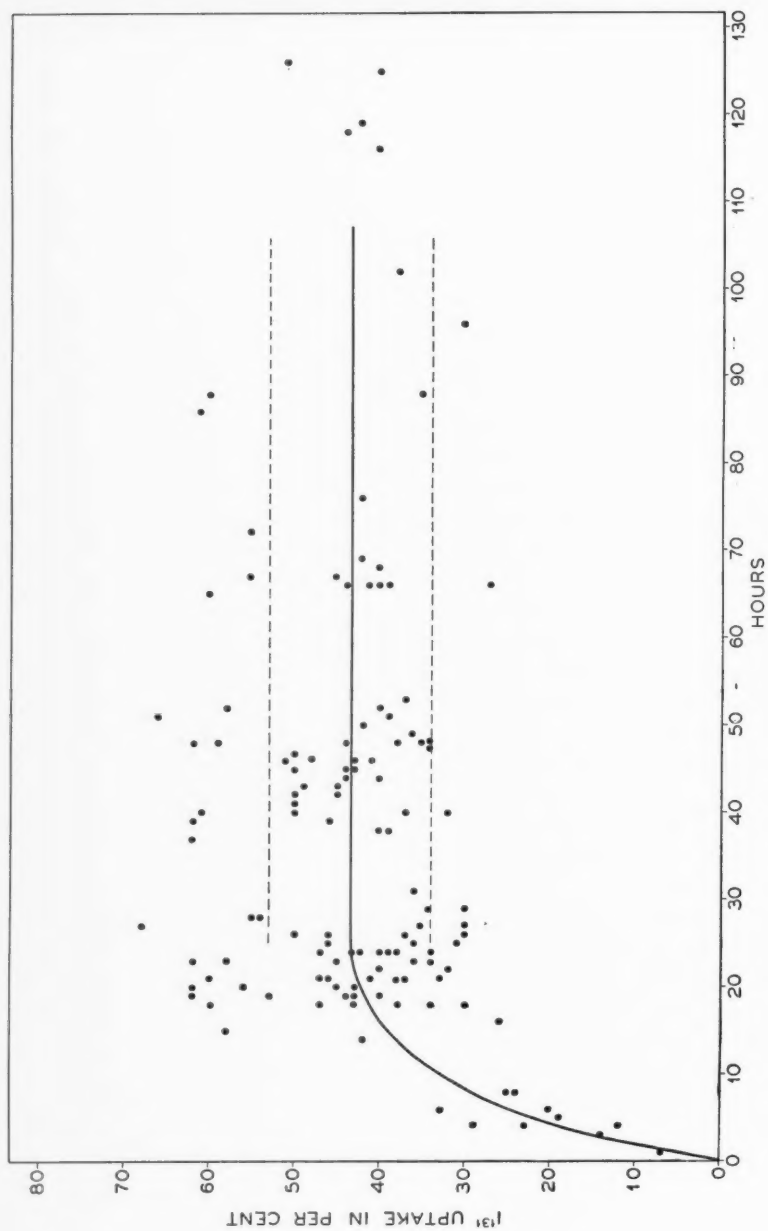


Fig. 1.

Percentage iodine 131 uptake over the thyroid gland in 44 euthyroid patients, showing the mean value (—) and standard deviation (---).

Chapter III

UPTAKE OF I¹³¹ IN THE THYROID GLAND OF CHILDREN WITH HYPOTHYROIDISM

PREVIOUS STUDIES

As mentioned, it was not until the introduction of tracer technique that some estimate could be made of the amount of active thyroid tissue in a large number of children with hypothyroidism. Measurements of the uptake of I¹³¹ over the thyroid gland are in themselves only an index of the amount of I¹³¹ which is found in the gland at that point of time. The glandular activity, whereby the hormone is produced, can be determined for one thing from the speed with which the hormone is released to the blood (conversion rate), this depending among other things on the TSH-stimulation. To determine the levels of radioactive iodine in the blood, larger amounts of radioactivity are required than the author was willing to make use of. However, in the more severe forms of thyroid hypoplasia, the gland seems to function at a maximum rate, so that the magnitude of the uptake presumably represents, at the same time, an estimate of the functioning of the gland.

Hamilton *et al.* (1943) were the first to show that some children with hypothyroidism can accumulate no or only a little I¹³¹ in the thyroid gland. They demonstrated this state of affairs in 8 out of 10 patients with severe hypothyroidism, aged 6 months to 19 years. Since then, numerous other workers have been able to confirm and extend these findings (Quimby & McCune 1947, Lowrey *et al.* 1949, Reilly & Bayer 1950 and 1952, Silverman & Wilkins 1953, Horst & v. Harnack 1953, McGirr & Hutchison 1953-54-55, Bernheim & Berger 1954, Andersen 1955, Tubiana & Ravaud 1956, Brante *et al.* 1956, Sheline *et al.* 1957, Wilkins 1957, Smith *et al.* 1957, Lowrey *et al.* 1958 and others).

From the studies mentioned, it appears that by far the majority of hypothyroid children without goitre, with symptoms from birth or during the first few months of life, show no or only insignificant uptake over the thyroid gland. Furthermore, it appears that in those children in whom this disease becomes manifest at a later point of time, some activity can be demonstrated, although sub-normal, and more or less proportional to the time elapsing before the onset of the symptoms (Silverman & Wilkins 1953, Horst & v. Harnack 1953,

McGirr & Hutchison 1955, Andersen 1955). Patients with sub-lingually retained thyroid tissue, as described in the next section, may be included together with this group of children. Finally, hypothyroid children with goitre constitute a special group, to be described later.

AUTHOR'S STUDIES

The material consists of all those children, a total of 56, with primary (thyrogenic) hypothyroidism, who were examined at Dronning Louise's Children's Hospital from the autumn of 1954 until the spring of 1959, i. e. the period during which the I^{131} test was employed.

The expression "*primary* thyrogenic hypothyroidism" is used as a definite designation for those patients who have ectopic thyroid tissue or goitre (see below, groups II and III). Should children with a *secondary* (hypopituitary) hypothyroidism occur in the material, these cases would be found presumably in group I, among children with an I^{131} activity of 10–15 % over the thyroid gland, as even total absence of thyrotropic hormone in the pituitary would hardly cause the thyroid activity to fall much lower, and at any rate not to zero. Among the 7 patients with an I^{131} uptake between 10 and 15 % (see table V, p. 41) there were in fact none of the hypopituitary dwarfism type, in whom a reduced TSH-activity is found together with other demonstrable signs of hypophyseal insufficiency, and which is only partly improved by thyroid treatment. Such patients have in general been excluded from the material. It is rare to find absence of TSH alone, without other symptoms. A condition such as this is excluded in two of the seven patients, as they showed no increased I^{131} uptake after stimulation with TSH. In the remaining five patients, extra dosage with I^{131} to exclude the possibility of secondary hypothyroidism was not considered indicated.

In none of the 56 patients with hypothyroidism is there anything in their history to suggest post-natal thyroid disease or trauma as a possible cause of their impaired thyroid function. It was therefore considered justified to designate the patients in group I as being athyrotic, or as having thyroid hypoplasias of varying degree. In one case, patient no. 2, an opportunity to verify the diagnosis of athyrosis was presented during an operation on the neck. In the remaining cases, thyroid biopsy was not found indicated.

All the children were hospitalised for longer or shorter periods, with the exception of case no. 25, who was examined as an out-patient. The majority of the patients were followed by the author for a longer period of time at the Endocrine Clinic of the hospital, the remainder are children from other hospitals, admitted for the examination. The information on these children originates from the respective case records, from X-rays and from discussions

with their parents. A summary of the case histories of patients no 1-56 will be found at the back on the following pages: cases no. 1-24, page 125-131, cases no. 25-38, page 132-137, and cases no. 39-56, page 137-144.

GROUPING OF THE PATIENTS

On the basis of clinical examinations and the results of I^{131} tests, the patients were grouped as follows:

Patients <i>without</i> enlargement of the thyroid gland (see fig. 2).	{	Group I: patients without any uptake or with reduced uptake of I^{131} over the thyroid gland	24
		Cases no. 1-24.	
		Group II: patients with exclusively sub- lingual, ectopic uptake of I^{131}	14
		Cases no. 25-38.	
Patients <i>with</i> enlargement of the thyroid gland (see fig. 7, p. 71).	{	Group III: patients with palpable, large or small goitre	18
		Cases no. 39-56.	
		Total	56

GROUP I: PATIENTS WITH APLASIA OR HYPOPLASIA OF THE THYROID GLAND

Fig. 2 shows the value of the I^{131} uptake for the patients of this group (cases no. 1-24): their data are recorded in table IV, page 38, according to when the diagnosis of hypothyroidism was made and the treatment with thyroxine started. In the majority of cases, it is possible to establish this time very precisely. In addition to the degree of severity of the disease, other factors are involved in fixing the time, such as the ability of parents (or others) to observe the child, and their delay before calling for medical assistance, as well as the experience of the physician in making the diagnosis. These factors must presumably apply to all the groups, even Group III, as early in the disease the goitre is often not recognised.

Generally speaking, the age at which the symptoms of the disease are first noticed is a very poorly defined point of time, being dependent also on the sharpness of both questioner and parents. In this connection attention will merely be drawn to the fact that constipation, for example, an early and frequent symptom in hypothyroidism, may have a cause other than this, so one should be careful when using this symptom to date the onset of hypothyroidism. The same is the case for failure to thrive, for umbilical hernia and for other early signs of hypothyroidism. On the other hand, the classic signs: macroglossia, myxoedematous skin and torpor, are often of rather late onset.

Table IV.
Group I: patients with aplasia and hypoplasia of the thyroid gland.
Cases no. 1-24.

Case no.	Sex	B. weight, g B. length, cm	Symptoms first noticed	Age at diag. and treatment	Treatment		Result		Iodine ¹³¹ test			
					duration	u. per day	phys.	mental	I. Q.	age	%/24 hrs.	tr. discont. before test
1	F	3500/51	0 mth.	10 days	8½ yr.	100-400 u.	N	R/N	90	6 yr.	0-1	6 weeks
2	F	3500/51	0-1 mth.	1½ mth.	5½ yr.	200-300 insuff. during 2nd & 3rd mth.	N	R	84	1½ yr.	0	not discontinued
3	M	3100/52	0-2 mth.	2 mth.	4 yr.	100-200	N	R	80	2½ mth.	0	untreated
4	F	3400/51	0-2 mth.	2 mth.	5½ yr.	100-600	N	R		5½ yr.	0	6 weeks
5	M	3400/51	0-2 mth.	2 mth.	19 yr.	200-400	N	R	55	15 yr.	0-2	6 weeks
6	F	3100/50	1-2 mth.	2 mth.	3 mth.	100 insuff.	N	N?		3 mth.	0-2	untreated
7	M	3250/52	1-2 mth.	2 mth.	2½ yr.	150	N	N		2½ yr.	10	7 weeks
8	F	4600/55	1-2 mth.	3½ mth.	4 mth.	200 insuff.	N	N?		4 mth.	0	untreated
9	F	3700/54	2-3 mth.	4 mth.	2 yr.	150-200	R	R		2½ yr.	3	4 weeks
10	M	3500/51	2-4 mth.	5 mth.	13 yr.	200	N	R		13 yr.	0	6 weeks
11	M	3200/48	2-4 mth.	5 mth.	18 yr.	200-600	N	R		14 yr.	6-7	2 weeks
12	F	3700/54	3-4 mth.	7 mth.	2½ yr.	200	N	R		2½ yr.	2-4	4 weeks
13	M	3500/51	3-6 mth.	10 mth.	2 yr.	200	N	R	52	3½ yr.	2-4	4 weeks
14	F	3600/54	0-6 mth.	1½ yr.	1½ yr.	100-300 insuff.	R	R		2 yr.	0	4 weeks
15	F	3200/51	1½-1 yr.	1½ yr.	7½ yr.	50-100 insuff.	R	R		9 yr.	5	8 weeks
16	M	3200/51	1-2 yr.	2½ yr.	5½ yr.	200-400	N	N	100	8 yr.	0	3 weeks
17	F	3500/50	1-2 yr.	3 yr.	5 yr.	200 insuff.	R	R		8 yr.	0	6 weeks
18	F	3400/53	4-5 yr.	5 yr.	5 yr.	200-400	N	R		5½ yr.	10	untreated
19	M	3600/52	2-3 yr.	5½ yr.	3 mth.	200 insuff.	R	R/N		5¾ yr.	10	untreated
20	F	3100/51	1-1½ yr.	6 yr.	6 yr.	100-200 insuff.	R	R		12 yr.	10	6 weeks
21	F	4000/56	1½-1 yr.	7 yr.	6 yr.	200-400	N	R		9½ yr.	5	3 weeks
22	F	3250/48	4-5 yr.	8½ yr.	1½ yr.	200-400	N	N	121	8½ yr.	15	untreated
23	M	4500/53	8-9 yr.	10 yr.	½ yr.	200 insuff.	N?	N		10½ yr.	14	6 weeks
24	F		10-11 yr.	12 yr.	5 yr.	400-600	N	N		17 yr.	12	12 weeks

N normal R retarded

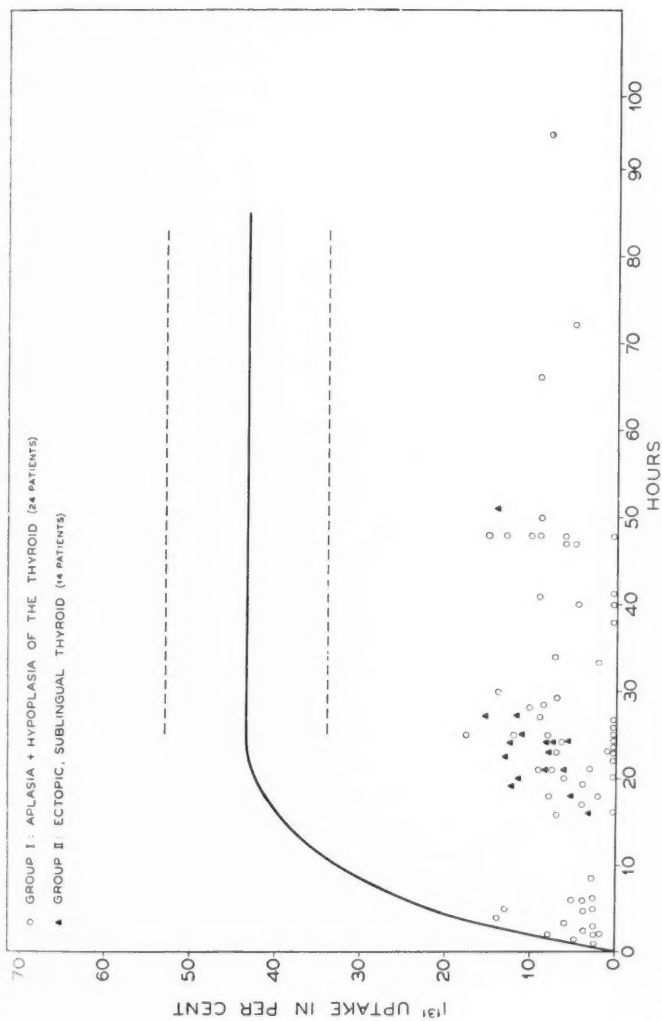


Fig. 2.
Percentage iodine¹³¹ uptake over the thyroid gland for patients in Group I and II, compared with the normal uptake curve.

THE MENTAL PROGNOSIS FOR PATIENTS IN GROUP I

The determination of intelligence, the age at diagnosis in relation to I^{131} uptake and the treatment will all be discussed, before evaluating the material.

The intelligence was determined on the basis of a general clinical evaluation, supplemented by information from parents, kindergartens, schools, etc. About half the children were also given an intelligence test on one or more occasions by the psychologist attached to the hospital. All the children were examined by the present author, the majority over an extended period of time.

In table V (page 41), the patients in Group I are classed according to the amount of radioactivity measured over the thyroid gland. The grouping into 5 % intervals is arbitrary, for one thing on account of the uncertainty of the small values found, so continuous transition between the adjacent groups must be anticipated. With the exception of three of the patients (cases no. 7, 16 and 17), who will be discussed later, there is *quite good correlation between the radioactivity measured, the age at onset of symptoms and the age at diagnosis*.

Patients with an uptake of 0–5 % have uniform features, as in the majority the disease becomes manifest in the course of the first three months of life, and within six months in the remainder.

In one of the three patients with an uptake of 5–10 %, the disease became manifest during the first six months, and in the others during the second six months of life.

All patients in the group with an uptake ≥ 10 % are found to have late "infantile" manifestation.

Exceptions: patient no. 7, with an uptake of 10 %, constitutes an exception, being diagnosed before the age of three months. As a baby, however, this patient was admitted to a paediatric department for other reasons, so that his chances of early diagnosis were therefore better than average.

The opposite is the case for patient no. 17. This patient was diagnosed later than would have been expected from her lack of I^{131} uptake. She is the youngest of seven siblings of harrassed, rather primitive parents who recall well enough that the patient developed somewhat later than the other children, but who, for various reasons, were lacking in more precise observation and earlier intervention.

Patient no. 16 appears to have been carefully observed at home and seemed to manage well until the age of about one year. In spite of the late commencement of treatment his intelligence is normal. Both these factors are unusual in a patient with an uptake of 0 %. Several similar examples are found in the literature without any explanation being available. It is possible that a thyroid atrophy commenced at the age of one year, but the personal history offers no grounds for invoking throat infections, traumas etc. as causal

Table V.

Mental development in patients of group I, divided according to iodine¹³¹ percentage uptake over the thyroid gland.

Case no.	0 % iodine ¹³¹		
	S.	D. & Rx	M.
2	0-1 mth.	1½ mth. (effective from 4 mth.)	R
3	0-2 mth.	2 mth.	R
4	0-2 mth.	2 mth.	R
8	1-2 mth.	3½ mth. (treated for 4 mth.)	N ?
10	2-4 mth.	5 mth.	R
14	0-6 mth.	1½ yr.	R
16	1-2 yr.	2 ⁹ / ₁₂ yr.	N
17	1-2 yr.	3 yr. (insufficient)	R
< 5% iodine ¹³¹			
1	0	10 days	R/N
5	0-2 mth.	2 mth.	R
6	1-2 mth.	2 mth. (treated for 3 mth.)	N ?
9	2-3 mth.	4 mth.	R
12	3-4 mth.	7 mth.	R
13	3-6 mth.	10 mth.	R
< 10% iodine ¹³¹			
11	2-4 mth.	5 mth.	R
15	½-1 yr.	1½ yr.	R
21	½-1 yr.	7 yr.	R
≥ 10% iodine ¹³¹			
7	1-2 mth.	2 mth.	N
18	4-5 yr.	5 yr.	N
19	2-3 yr.	5¼ yr. (insufficient)	N
20	1-1½ yr.	6 yr. (insufficient)	R
22	4-5 yr.	8 ⁹ / ₁₂ yr.	N
23	8-9 yr.	10 yr. (insufficient)	N
24	10-11 yr.	12 yr.	N

S = symptoms first noticed.

D = time of diagnosis.

Rx = start of thyroid treatment.

M = mental development (N = normal, R = retarded).

factors. In this patient, the possibility of ectopic thyroid tissue can be excluded, as he was examined with this in mind in the same way as all athyroid patients. The third possibility, which at any rate cannot be excluded as far as the present author is concerned, although he has not noticed similar cases, is faulty technique, confusion of samples with rinsing water, etc.

The duration of the treatment and the magnitude of the dosage are shown in table IV. The concept "*adequate treatment*" is difficult to define, and opinions are divided on this. Various dosage schemes are recommended for the different ages. A procedure such as this can lead to unfortunate results. Quite considerable individual differences can occur, and it is considered that too rigid dosage schedules should not be followed. Just as in diabetes, where one does not adjust the dosage according to the age of the children either, an attempt should be made to reach an individual dosage, based on the condition of the child and on certain measurable criteria such as growth in height, bone and tooth development, PBI and serum cholesterol. Perhaps more important than anything else, the children should be observed frequently at first, for example once every three to four weeks, until the dosage is established. To begin with, a heavy dosage is employed until signs of overdosing appear, the dose then being reduced a little, although raised from time to time as need increases. There are seldom great difficulties in achieving a dosage scheme on which the children quite soon become somatically euthyroid, provided control is frequent and there is some experience of hypothyroid children.

Certain authors have warned against so powerful a medication that a bone age is achieved which surpasses the actual age. Since the "optimal dosage" is not known with certainty, and as it is still the general opinion that under-dosing is harmful, at any rate during the first period of the treatment, the author has chosen to medicate as indicated even though in some cases skeletal maturation is strongly accelerated as a result. The point of view is that an effort should be made to obtain as great an intellectual development as possible, even if at the expense of the final height. Furthermore, the concept of bone age is a very fluid one in hypothyroid children at this stage, as the various parts of the skeleton show varying rates of reaction to treatment. As *Wilkins* has stressed, quite another fact is that if after some time it is obvious that the child will remain retarded, its treatment should be so arranged as to result in an amenable, possibly slightly hypothyroid child, rather than an irritable, more or less subtoxic one.

Table IV thus shows the treatment given on the above lines. Where treatment has either been poorly arranged according to our views, where too low dosage has been used, not achieving a normal somatic development even after many years, or where treatment has been of brief duration, this has been indicated by "insufficient".

Development of the intelligence in relation to the time of commencement of treatment, dosage and I^{131} uptake.

If one selects those children treated within the first three months of life, the group consists of the following patients (R = retarded, N = normal): Cases no. 3 (R), 4 (R), 1 (R/N), 6 (N)?, and 7 (N). Of these, the first two are retarded and the third is a borderline case (I. Q. 90), in spite of early diagnosis and treatment. The fourth patient promises to develop normally, but a period of observation of three months is too brief for a final evaluation. The fifth patient (case no. 7), who became mentally normal, has been discussed previously, page 40. In this patient, the thyroid tissue present at birth ($\geq 10\%$ activity) has presumably had the same effect as an early treatment, in contrast to the remaining patients in this group, who all have $< 5\%$ uptake.

As a whole, the prognosis appears to be poor in athyrotics even with early treatment, though not completely hopeless.

Those patients who received treatment from the age of three months and up to three years, all have uptakes of less than 10% : case no. 2 (who received brief treatment at the age of one to two months) (R), 8 (N?), 9 (R), 10 (R), 11 (R), 12 (R), 13 (R), 14 (R), 15 (R), and 16 (N). In spite of regular and vigorous therapy from the time of diagnosis, the only ones who became normal are patient no. 8, whose period of observation—4 months—is insufficient for a final evaluation, and the oldest patient in the group, no. 16. *If the mental development is to proceed successfully in athyrotics or patients with severe hypoplasia, it seems that treatment must be commenced not later than around the fourth month of life.*

Considering the group treated later than the age of three years, this includes the following children: case no. 17 (R) (insufficient treatment), 18 (N), 19 (N) (insufficient), 20 (R) (insufficient), 21 (R), 22 (N), 23 (N) (insufficient) and 24 (N). The condition of patients no. 17 and 21 was not only ignored by their parents but, in addition, they had little or no thyroid tissue. The remainder of the patients had in fact activities $\geq 10\%$. Of these, only case no. 20 is retarded (exceedingly neglected treatment with symptoms from $1\frac{1}{2}$ –6 years of age prior to the commencement of treatment). The remainder are of normal intelligence, no. 19 and 23 being so in spite of insufficient treatment.

Thus, Murray's statement in 1900, hardly 20 years after the clinical picture was recognised, still holds: "The shorter the duration of the disease at the commencement of treatment, the more rapid is the improvement in the mental condition; I believe that only in those cases whose treatment has commenced early can we expect a normal intellectual development to take place."

The converse question, why the majority of those patients treated early do *not* become normal, seems to be more difficult to explain.

It will be seen from the previous discussion (p. 15) that two main points of view have been operative. One is that in addition to their hypothy-

roidism, the children have cerebral damage or an intelligence defect, while the other is that in certain cases, prenatal hypothyroidism or the early onset of post-natal hypothyroidism manages to cause permanent maturation defects in the central nervous system before the commencement of thyroxine treatment. In the present material, the author has been unable to demonstrate the severe E. E. G. changes (dysrhythmias) found in certain patient series to quite a considerable extent (see p. 16), particularly in those showing severe mental damage, and regarded as a sort of proof of primary cerebral defect. However, only about half of the cases had an E. E. G. taken. In certain of our patients, even those untreated, no more than slight dysrhythmias have been demonstrated, of no definite pathological significance, and in a number of cases merely a slow alpha rhythm, usually occurring in hypothyroid patients and disappearing during treatment. It is also conceivable that in some of the severe cases the E. E. G. changes are sequelae of secondary and not primary cerebral changes. There is no doubt that electroencephalograms should be taken to a greater extent than we have been able to do in our material. On the other hand, however, the value of an E. E. G. for demonstrating such widespread and profound changes as can be expected in this disease, is presumably limited.

FURTHER STUDIES OF THE PATIENTS IN GROUP I

Aplasia and hypoplasia of the thyroid gland in relation to the age of the parents.

The age of the parents is recorded in the case histories. The present material does not appear to show any correlation between the age of the parents, particularly that of the mother, and the frequency of the disease, as is found for example in mongolism.

The influence of pregnancy and birth on aplasia and hypoplasia of the thyroid gland.

According to the information collected, complications appear to have been present in only one pregnancy (case no. 13, where a uterine fibroma was removed during pregnancy). A positive toxoplasmosis reaction was found in mother and child in patients no. 2 and 45, without any clinical sign of toxoplasmosis infection. The parents of patient no. 9 are cousins, a relationship reported with striking frequency in the literature.

Delivery appears to have been normal in these children, but it is striking that a number of mothers have remarked that the child was "born too late". So far we have no exact material to elucidate this question.

The birth-order of the child. In this group, there are 16 first-born out of a total of 23 children, information not being available in case no. 14. The proportion (70 %) is higher than that found in the general population, but the figures were felt to be too limited for any conclusion as yet.

Associated congenital malformations or the like were found in patient no. 7, operated on for intestinal stricture and for club foot. Case no. 15 has cerebral palsy (athetosis), observed at about the age of one year.

Serum cholesterol was determined in practically all the children at one time or another. The results correspond to those usually quoted: elevated values in the majority of those untreated or after a withdrawal period of 4-6 weeks, with the exception of children during the first few years of life, when values of less than 200 mg% may be found.

Protein-bound iodine (P. B. I.) was determined in more than half the patients in this group. Case no. 2 and case no. 19 showed normal values and case no. 12 had elevated values. The remainder of the determinations in the untreated children, or after withdrawal of thyroxine for 3-6 weeks, were low.

ATHYROTIC PATIENTS WITH SIGNS OF PRE-NATAL HYPOTHYROIDISM

a) Bone development

The material includes children tested with I^{131} at the time when the diagnosis was made, as well as children tested several years after the diagnosis. For both these categories, there is in general the same correlation between the time of manifestation of the disease and the uptake (see cases no. 3, 4 and 5 in table IV p. 38). It may presumably be concluded from this that the uptake over the thyroid gland at a given point of time is in essential respects a measure of the effectivity of the gland at birth, and probably also during the last stage of foetal life. There is still not enough information on the cause or causes of athyrosis to permit any definite statement on the early foetal thyroid function, but it does not appear likely that birth in itself should result in total or almost total termination of thyroid function.

Another question which will be discussed in greater detail later (p. 106) is whether patients with no or only slight uptake have been hypothyroid in foetal life or whether their requirements have been covered by the thyroid function of the mother.

Dorff (1934), in his twin study (see p. 85), showed that the bone centres of the twin with hypothyroidism had only prenatal development, while the other twin was normal. He concluded that the maternal coverage of thyroid hormone requirements was insufficient, and that the foetus was dependent to a considerable degree on its own thyroid function. These points of view were subsequently stressed and developed by *Wilkins* and *Hutchison & McGirr*, among others.

Table VI.
Athyrotic patients with evidence of pre-natal hypothyroidism.

Case no.	B weight, g B length, cm	Symptoms first noticed	Diagnosis and treatment	Bone development	Dental development	Mental development	Iodine ¹³¹ percentage
2	3500/51	0-1 mth.	1½ mth.	at 4 mth.: Distal ossification centre of femur only just visible, with dysgenesis. Prox. tibial centre and centre for cuboid both missing (Sufficiently treated from 4 mth.).	at 4¾ yr.: Bone age 5 yr. Dental age 4½ yr. Hypoplasia of enamel of in- trauterine type.	R (I. Q. 84)	0
3	3100/51	0-2 mth.	2 mth.	at 2 mth.: Distal centre of femur, prox. centre for tibia and centre for cuboid all missing.	at 2 yr.: Bone age 2 yr. Dental age 2 yr. Hypoplasia of enamel of intrauterine type.	R (I. Q. 80)	0
6	3100/50	1-2 mth.	2 mth.	at 2 mth.: Distal centre of femur, prox. centre for tibia and centre for cuboid all missing.	at 2 mth.: Dental age according to X-ray was "minus 1 mth."	N? (Treated 3 mth.)	0-2
8	4600/55	1-2 mth.	3½ mth.	at 3½ mth.: Distal centre of femur and centre for cuboid just visible, dysgenetic. Prox. tibia centre missing.	at 4 mth.: Dental age according to X-ray was 0-2 mth.	N? (Treated 4 mth.)	0

Author's studies.

In four (cases no. 2, 3, 6 and 8) of the eight patients (cases no. 1-8) in whom the diagnosis was made within the first $3\frac{1}{2}$ months of life, there are X-ray pictures showing prenatal bone development. In the remaining four patients this condition cannot be determined, as the exposures available, particularly those of the wrist and ankle, are unsuitable for such prenatal dating.

Table VI shows the results of the bone centre studies made on the four children mentioned. These children were all of normal weight at birth, so that the absence of distal femur centres in cases no. 3 and 6 must be regarded as proof of a condition of prenatal bone development, (Christie 1957) (see p. 85). In no. 2 and 8, who were both about four months of age at the time of the first X-ray examination, and of whom no. 2 was treated shortly before this at the age of $1\frac{1}{2}$ -2 months, the just visible "dysgenetic" femur centres presumably also suggest prenatal hypothyroidism (figs. 3, 4 and 5).

According to *Wilkins*, dysgeneses of this kind must be regarded as being specific, but the difficulties of using bone centre development for dating an intrauterine hypothyroidism are that the changes are blurred with time, and particularly after a brief treatment.

b) Enamel hypoplasias of intrauterine origin in children of Group I.

The enamel of the teeth was studied in an attempt to find other, more permanent signs of intrauterine disturbance of growth in these children. The studies suggest that the dental development in a number of these children has suffered intrauterine damage. The question will be discussed further on page 104.

c) Growth in height of athyrotic children.

Thus, while there seems to be good reason to assume that as far as bone development and dental development are concerned, at any rate some athyrotic patients are prenatally hypothyroid, the third of the cardinal somatic signs of hypothyroidism, growth in height, does not appear to fit in with this assumption.

Horst and *v. Harnack* (1953), *Flamand Christensen* (1956) and *Childs & Gardner* (1954), draw attention to the fact that a number of hypothyroid children are over-weight at birth. However, as far as the present author can see, exact figures for birth length of hypothyroid children are not given in the literature, although *Hurxthal* (1948) reports normal conditions.

An inspection of table IV (p. 38), in which birth weight and birth length are given, together with the time of manifestation of the disease, shows that with one exception, cases of hypothyroidism presenting early are of normal or more than normal length at birth. Furthermore, the weight is also considerably greater in a number of these children. Only case no. 25 is a true premature, less than 2500 g.

Examples of prenatal bone development in athyrotic patients.



Fig. 3.

Case no. 6. Two-month-old, untreated. Distal ossification centre in the femur, and proximal ossification centre in the tibia, are both missing.

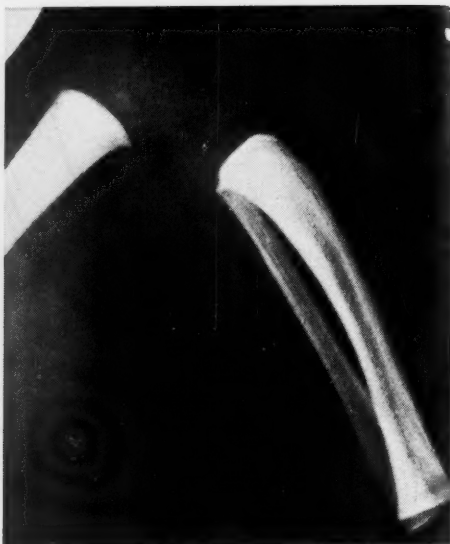


Fig. 4.

Case no. 8. 3 1/2-month-old, untreated. Distal ossification centre in the femur just visible with dysgenesis. Proximal ossification centre missing in the tibia.

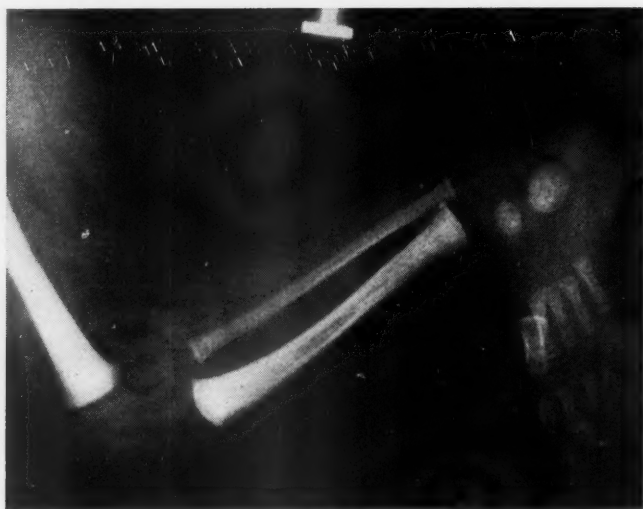


Fig. 5.

Case record no. 768/53. Three-month-old athyrotic patient, untreated. Picture shows absence of distal femur and proximal tibia ossification centres and centre for the cuboid. This patient also had congenital toxoplasmosis, and the diagnosis of aplasia of the thyroid gland was confirmed at autopsy.

What actually makes the athyrotic foetus grow and develop, does not seem to have been elucidated. On the face of it, hormonal influence from the mother, from the placenta, from the foetus itself, or combinations of these, might be considered.

Among the hormones from the mother, thyroid hormone must be considered in the first instance. As is known (*Grumbach & Werner, 1957*), thyroxine can pass through the placenta, although in small amounts. In hypothyroidism the growth in height *after birth* is retarded to a lesser degree than the bone development, but except in hypothyroidism of brief duration, the growth in height is *always* retarded. Such hypothyroidism of brief duration and late intrauterine origin could explain the findings in athyrotic children, although it agrees poorly with the fact that certain cases at birth are *longer* than normal. Other studies, particularly the twin studies mentioned on page 106 tell against transference of thyroid hormone from mother to foetus to any great extent. Hormones such as growth hormone, or androgenic and oestrogenic hormones from mother and placenta, would hardly give normal or vigorous growth in length in connection with delayed bone development.

If the conditions in the foetus are considered, thyroid hormone can naturally be excluded. The hypophysis in athyroid patients is hypertrophic, but we know from monkey experiments made by *Lusted et al. (1953)*, and from studies of the cranium in severely hypothyroid children (large sella), that this hypertrophy continues during the years after birth. Thus, as the growth of the newborn athyrotic child is already very inhibited shortly after birth, it is presumably not the hypophysis which determines intrauterine growth. A possibility being studied is whether the adrenal medulla, which is very big in normal foetuses and also in newborn athyrotics (*Kraus 1929*), but whose foetal zone atrophies considerably immediately after birth and has almost disappeared at the same time as the growth of the athyrotic child stops, produces substances with a growth-promoting and, to a lesser degree, bone-maturing action. The hormone production of the foetal adrenal medulla is still relatively unknown (*Gardner, 1956*).

There are undoubtedly other possibilities, and continued studies of foetal endocrinology will presumably elucidate the above questions.

Chapter IV

UPTAKE OF I^{131} IN CHILDREN WITH SUBLINGUAL THYROID TISSUE

THE FOETAL DEVELOPMENT OF THE THYROID GLAND

The description which follows is based in particular on the handbooks by *Minot* (1892), *Frazer* (1940) and *Hamilton et al.* (1945).

The development of the thyroid gland takes place from a median unpaired primordium which forms an outpocketing ventrally from the floor of the pharynx anterior to the tuberculum impar, when the embryo is about 3 mm long. This primordium follows the large vessels caudally as a diverticulum and becomes sited anteriorly to the trachea. At the 5 mm embryo stage, the glandular tissue forms a rather thin transverse mass, which then differentiates into two lobes with an intermediate isthmus. At about the 10 mm embryo stage the connection between the point of origin and the gland (ductus thyroglossus) becomes atrophied, and remains dorsally as the foramen coecum linguae and ventrally as the lobus pyramidalis, in a few cases together with larger or smaller amounts of disrupted cellular remains along its course. Shortly after this a confluence takes place with two lateral primordia, which grow forward from the fourth branchial pouch. The significance of these later components is unknown. As *Horst & von Harnack* (1953) have stressed, studies of the sub-lingually retained thyroid tissue, which will be mentioned later, tell against the possibility that the lateral primordia themselves can form functional glandular tissue.

PREVIOUS INVESTIGATIONS OF SUBLINGUAL RETENTION OF THE THYROID GLAND

In 1953, *Horst & von Harnack* published an excellent but rarely quoted study of the forms of hypothyroidism and their differentiation in children, based on examinations using I^{131} . This study contains the first description known to the present author of sublingual uptake of I^{131} as the sole localisation in two hypothyroid children without goitre or any other palpable thyroid tissue. The

patients were 2 years 3 months and 3 years 5 months of age, with a somewhat slow course of their disease, which was diagnosed at the ages of 2 years 3 months and 2 years 9 months respectively. The one patient was also remarkable by being a monozygotic twin, with a healthy twin partner, children of a mother who developed Graves' disease during pregnancy. The mother of the other patient developed Graves' disease during an earlier pregnancy.

Similar cases were described independent of each other in the subsequent period. Thus, at the radiological conference in London in the summer of 1954, *Allen et al.* demonstrated a "gammagram", which showed exclusively sub-lingual accumulation of I^{131} in a 9-year-old boy with "infantile" hypothyroidism of slow onset.

McGirr & Hutchison (1954) described the case of a 7½ year old girl with untreated infantile hypothyroidism. The patient had been constipated from birth and increasingly retarded in growth from the age of 3 years, but had normal intelligence with good scholastic ability. Studies with I^{131} showed an uptake over the basis linguae of about 30 % of the amount administered, but none at the normal site of the thyroid gland, where no glandular tissue could be demonstrated either. The investigators were led on the track of this

Table VII.

Previously reported cases of patients with sub-lingual, ectopic thyroid tissue, diagnosed by iodine¹³¹.

Author	Year	Sex	Age at exam.	Symptoms first noticed	Age at diagnosis	Percentage iodine ¹³¹ (24 hrs.)
Horst, W. & G. A. v. Harnack	1953	F	2½/12 yr.		2½/12 yr.	3
Horst, W. & G. A. v. Harnack	1953	F	5¾/12 yr.		3¾/12 yr.	0.2
McGirr, E. M. & J. Hutchison	1954	F	7¾/12 yr.	3 yr.	app.	30
					7¾/12 yr.	
Allen, H. C. et al.....	1954	M	9 yr.		9 yr.	
McGirr, E. M. & J. Hutchison	1955	F	4¾/12 yr.		4¾/12 yr.	14
Neimann, N. et al.....	1958	M	9 yr.	6 yr.	7¾/12 yr.	3
Neimann, N. et al.....	1958	M	5 yr.	5 mth.	5 mth.	3.8
Neimann, N. et al.....	1958	F	2¾/12 yr.	3 mth.	3 mth.	3.5
Neimann, N. et al.....	1958	F	8 yr.	2 yr.	2¾/12 yr.	3.7
Neimann, N. et al.....	1958	F	2 yr.	3 mth.	6 mth.	4.5
Neimann, N. et al.....	1958	F	6 yr.	1 yr.	4 yr.	4.8
Neimann, N. et al.....	1958	F	12 yr.	6 yr.		5
Neimann, N. et al.....	1958	F	2¾/12 yr.	1½/12 yr.	1¾/12 yr.	6
Neimann, N. et al.....	1958	F	8 yr.	5 yr.	3¾/12 yr.	6
Neimann, N. et al.....	1958	F	8 yr.	4 yr.	6 yr.	9
Neimann, N. et al.....	1958	F	8 yr.	4 yr.	5 yr.	9
Neimann, N. et al.....	1958	F	2 yr.	1 yr.	8 yr.	12.7
Neimann, N. et al.....	1958	F	27 yr.	1 yr.		14
Neimann, N. et al.....	1958	F	29 yr.	1-2 yr.		23

localisation by the fact that a previously examined patient who had developed hypothyroidism after the removal of a thyroglossal cyst containing thyroid tissue, accumulated I^{131} only over the site of operation and not at the normal site. *McGirr & Hutchison* stress the significance of this technique of investigation in clarifying the pathogenesis in certain forms of "juvenile" hypothyroidism.

In the spring of 1955, the present author was able to demonstrate the presence of a corresponding condition in an infant of 7 months with "congenital" hypothyroidism of rather slow progression. The clinical picture was compared with that of two hypothyroid infants with early clinical manifestation and no accumulation of I^{131} at any site. In one of these children (case no. 2) the diagnosis of *athyrosis* was later verified operatively on the occasion of the removal of a thymus tumour.

Only few reports of sublingual retention have been communicated since then (see table VII), so that the literature gives the impression that this pathogenesis is rare, or at any rate is rarely found.

During the preparation of the present study, a paper was published by *Neimann et al.* (1958), in which 14 cases of sublingual retention of thyroid gland are described (12 in children aged 2-12 years and 2 in adults).

AUTHOR'S INVESTIGATIONS OF SUBLINGUAL RETENTION OF THE THYROID GLAND (GROUP II)

This group of 14 patients out of a series of hypothyroid children studied, 56 in all, constitutes a remarkably large number in comparison with the reports in the literature, from which one almost gains the impression that these patients are curiosities. However, as mentioned already, the fact that *Neimann et al.* (1958) in France have been able to find a similar number almost within the same period of time, is hardly the result of local phenomena, but is more likely to be the result of a routine examination for ectopic thyroid tissue in all hypothyroid patients who showed little or no I^{131} activity over the normal site of the thyroid. Had this procedure not been used, the patients in question would have been classified as athyrotic.

Table VIII shows that only two patients were diagnosed at an early age (less than six months), and these two resemble athyrotics clinically, while the remaining 12 correspond clinically to cases of hypoplasia, as one would also have expected. These patients also show a fairly good correlation between the thyroid activity and the time of occurrence of symptoms. The high uptake percentage in the child whose disease was diagnosed earliest, is remarkable. There may be technical reasons for this, but other circumstances may be involved. This child is the only patient in the entire material who was known with certainty to have had such prolonged severe icterus neonatorum that this

Table VIII.

Group II: patients with ectopic, sub-lingual thyroid gland.
Cases no. 25-38

Case no.	Sex	B. weight, g B. length, cm	Symptoms first noticed	Age at diag. and treatment	Treatment		Result		Iodine ¹³¹ test			
					duration	unit/day	phys.	mental	I. Q.	age	%/24 hrs.	tr. discont. before test
25	F	2450/50	0-1 mth.	1 1/2 mth.	0	0	R	R		2 mth.	12	untreated
26	M	4700/57	0-1 1/2 mth.	3 mth.	5 yr.	200-400	N	R	84	1 1/2 yr.	3	4 weeks
27	F	3200/49	4-5 mth.	7 mth.	4 yr.	200-300	N	N	> 90	7 mth.	6	untreated
28	F	4000/51	6-12 mth.	14 mth.	11 yr.	100 insuff.	R	N		12 1/2 yr.	6	not discont.
29	F	4000/	1-1 1/2 yr.	1 1/2 yr.	10 yr.	100	N	N		13 yr.	13	6 weeks
30	F	3700/52	6-9 mth.	1 1/2 yr.	10 yr.	100-200	N	N		10 yr.	7	6 weeks
31	M	4150/53	1-1 1/2 yr.	1 1/2 yr.	10 yr.	100-200 insuff.	R	N	100	10 yr.	12	3 weeks
32	M	4150/53	6-7 mth.	1 3/4 yr.	13 yr.	200 insuff.	R	N	> 100	13 yr.	11	3 mth.
33	F	4150/53	5-6 mth.	1 3/4 yr.	3 1/2 yr.	300-400	N	N		1 3/4 yr.	8	untreated
34	M		3-6 mth.	4 yr.	9 yr.	300	N	N	81	13 yr.	11	3 weeks
35	F	3200/51	6-12 mth.	4 yr.	6 yr.	200	N	N		10 yr.	5	6 weeks
36	F	4050/53	1-1 1/2 yr.	4 1/2 yr.	200 insuff.	200	R	N ?		4 1/2 yr.	11	untreated
37	M	4200/54	3 yr.	6 1/2 yr.	1 3/4 yr.	300-400	R	N		6 1/2 yr.	15	untreated
38	F		1 yr.	8 1/2 yr.	5 1/2 yr.	100 insuff.	R	N	> 100	14 yr.	7	3 mth.

gave rise to an early suspicion of hypothyroidism, as pointed out by Åkerén (1954).

Age of the parents and course of pregnancy and delivery do not differ from what was found in the children with athyrosis and hypoplasia in Group I.

The birth-order of the child. In this group, there were 8 first-born out of a total of 14 children. The same considerations hold as discussed for Group I, p. 44.

Familial disposition to thyroid disease is only slightly pronounced, as in the patients of Group I. The familial incidence of hypothyroidism will be discussed later in the section dealing with goitrous hypothyroidism.

As table VIII shows, the mental prognosis for children with sublingually retained thyroid tissue is good, 10 of the patients becoming normal, three of them even being particularly intelligent (cases no. 29, 30 and 35). Two patients are retarded, case no. 26, whose disease became manifest early and corresponds to an athyrosis, and no. 34, who showed early symptoms but was treated late. Two patients (cases no. 25 and 36), untreated in the one case and treated for too short a time in the other, could not be evaluated, although case no. 36 promises to develop normally.

Thus, as far as the mental prognosis is concerned, these patients can be classed with the patients who have slight to moderate hypoplasia in Group I, and in whom the amount of thyroid tissue present at birth was presumably enough to bring them safely through the perinatal period which is so fateful for brain development. *A certain amount of sublingual thyroid tissue thus appears to be a prognostically favourable sign.*

Prenatal hypothyroidism in patients with sublingual, ectopic thyroid

As with the patients in the first group, a table has been set up (table IX) for the bone centre development and enamel hypoplasia etc., in those patients (a total of ten) with sublingual, ectopic thyroid for whom there are radiological studies to permit an evaluation of the prenatal development, and/or who have had dental studies made to assess hypoplasia of the enamel.

Bone centre studies. Patient no 25 was premature (2450 g), at the limit of normal birth weight, and the X-ray findings at the age of one month suggest prenatal hypothyroidism. In patients 26 and 27 the findings point in the same direction, although stippled bone centres can occur in normal subjects.

Dental studies (table IX). In those in whom a diagnosis was made early, as in the patients with athyrosis and hypoplasia of Group I, dental studies show the occurrence of enamel hypoplasias of intrauterine origin only. In the case of those children whose diagnosis was made later, it is obvious that the majority have avoided the intrauterine type. The time of onset for the enamel hypoplasias of postnatal origin agrees well with the onset of the hypothyroid signs, but as mentioned before, the majority of enamel hypoplasias of other

Table IX.
Bone and dental development in patients with ectopic, sub-lingual thyroid gland.

Case no.	B. weight, g B. length, cm	Symptoms first noticed	Diag. and treatment	Bone development		Dental development			Mental development
				Age		Age	B. A.	D. A.	H. E.
25	2450/50 (prema- ture)	0-1 mth.	1½ mth.	1 mth.	Bone centres for knee and cuboid missing.	3¾ yr.	4 yr.	3 yr.	R. (untreated)
26	4700/57	0-½ mth.	3½ mth.	3½ mth.	Distal femur centre v. small with dysgenesis. Prox. tibia centre just visible. Centre for cuboid missing.	3½ yr.	3½ yr.	3 yr.	R/N (I. Q. 84)
27	3200/49	4-5 mth.	7 mth.	7 mth.	Distal femur centre, prox. tibia centre just laid down, with dysgenesis. No centre in carpus.	12 yr.	11 yr.	10 yr.	N (I. Q. > 90)
28	4000/51	6-12 mth.	14 mth.			13 yr.	13 yr.	12 yr.	N
29	4000/	1-1½ yr.	1½ yr.			10¾ yr.	10-11 yr.	10-11 yr.	N
30	3700/52	8-9 mth.	1½ yr.	1½ yr.	Bone development: 3-5 mth. + dysgenesis.	10 yr.	4-4½ yr.	8 yr.	N
31		1-1½ yr.	1½ yr.			13 yr.	11 yr.	11 yr.	N
32	3000	6-7 mth.	1¾ yr.	1¾ yr.	Bone development: 0-3 mth. + dysgenesis.	2¾ yr.	2 yr.	2 yr.	N
33	4150/53	5-6 mth.	1¾ yr.	1¾ yr.	Bone development: 0-3 mth. + dysgenesis.	6½ yr.	6-12 yr.	4 yr.	N
37	4200/54	3 yr.	6½ yr.		Bone development: ½-1 yr. + dysgenesis.				

H. E. = type of hypoplasia of enamel.

D. A. = dental age.

B. A. = bone age.

origin occur just at this age, so the findings must be evaluated with this in mind. The bone centre development and intrauterine enamel hypoplasia in patient no. 37, whose diagnosis was made at a late stage, suggest that at any rate these tissues were affected early, and it seems surprising that his mental condition is so good.

Birth length and birth weight. In the first two patients, cases no. 25 and 26, who clinically and otherwise bear most resemblance to athyrotic cases, the birth length, as in such cases, is strikingly great, 50 cm being more than expected in a premature infant, and 57 cm being considerably more than the mean value for newborn (51 cm).

SEX DISTRIBUTION IN PATIENTS WITH SUBLINGUAL RETENTION OF THYROID TISSUE

On comparing the present material of patients with sublingually retained thyroid tissue with other series (*Neimann, Horst & v. Harnack, Hutchison & McGirr*), the present author was struck by the fact that the majority of these patients in the collected series are girls, and the overall sex distribution is 2:1. This is the distribution usually quoted for the sex incidence in children with hypothyroidism (eg. *Lowrey* 1958), without any explanation being available.

Now, the sublingual ectopic hypoplasias and the "topical" hypoplasias, as well as the aplasias, can probably be regarded in most cases as varying degrees of congenital malformation (dysgenesis); it therefore appears reasonable to regard these groups under one heading, and for the time being omit cases with goitre, which as will be mentioned later presumably constitute a group quite on their own, with a strong hereditary component, for one thing.

If tables IV and VIII are compared, girls are seen to be in the majority, 24 girls to 14 boys or approximately 2:1. Divided according to time of diagnosis into the first six months of life and later, the results for Groups I and II together are as follows:

Diagnosed within first 6 months: 6 boys and 7 girls.

Diagnosed after 6 months: 8 boys and 17 girls.

One thus finds a ratio of approximately 1:1 for the cases of early manifestation, and a ratio of approximately 2:1 for girls to boys for those cases diagnosed after the age of six months. In themselves the figures are presumably too small for definite conclusions, but if those series are examined which can be divided along more or less the same lines, omitting the cases with goitre, a corresponding state of affairs is found, a tendency which is reflected in the collected series of table X.

Table X.

Sex distribution in patients with non-goitrous hypothyroidism.

	Diagnosis \leq 6 mth.		Diagnosis $>$ 6 mth.	
	M	F	M	F
d'Avignon & Melin 1949	5	7	3	7
Radwin et al. 1949.....	3	1	4	4
Horst & v. Harnack 1953	5	3	0	7
Cooke et al. 1956.....	5	6	4	7
Neimann et al. 1958....	2	5	0	7
Andersen 1959.....	6	7	8	17
Total..	26	29	19	49

$\chi^2 = 4.09$ ($f = 1$) is found for the difference between the percentage of boys in the groups diagnosed before and after 6 months of age, a probability of less than 5%.

Chapter V.

PATIENTS WITH HYPOTHYROIDISM AND GOITRE

IODINE METABOLISM AND HORMONE PRODUCTION IN THE THYROID GLAND

What follows is to a considerable extent based on information in the chapter by J. B. Stanbury in the W. H. O. report on Endemic Goitre, vol. 18, no. 1-2, 1958.

In parts of the world where no endemic goitre exists, the daily intake of iodine in the diet of an adult is reported as being around 75-200 μg , and presumably somewhat less for a child. Most of the iodine is found in inorganic form, a smaller part as organic iodine compounds, which are reduced to inorganic iodide prior to absorption. Thyroxine, triiodothyronine and diiodotyrosine may be absorbed intact. The amount of iodide in the blood is very low, and has a volume of distribution of about 25 per cent of the body-weight. With the exception of the cells of the thyroid gland and the red blood cells, only minimum amounts of iodine enter the cells.

The iodide of the blood is either excreted by the kidneys or taken up by the thyroid gland. The ratio between these two processes determines the amount of iodine taken up by the gland. The kidneys clear the iodide in approximately 35 ml plasma per minute. This magnitude is not altered by iodine deficiency. The iodide clearance by the thyroid gland is about the same magnitude, and thyroid function tests using I^{131} are based on these conditions.

The ratio between the iodide content of the serum and of the thyroid gland is normally about 1:20, but can alter strongly in pathological conditions, for example in goitre. The iodide of the thyroid gland is found both in the epithelial cells and in the colloid, and can pass into the blood. Various processes may inhibit this release of iodine, and it can be accelerated by administration of thiocyanate or perchlorate, for example. The exchange between thyroid gland and blood seems to depend on properties of the epithelial cells. The iodide in the thyroid gland becomes oxidized, presumably as the result of a specific oxidative system in the thyroid cells, and immediately becomes bound at the 3-position (monoiodotyrosine) or at the 3- and 5-positions (diiodotyrosine) of the benzene ring of tyrosine residues, which occur in the

thyroid gland in peptide linkages. This step in the synthesis can be blocked by thiouracil compounds. A special tyrosine-oxidase has been described which seems to take part in the formation of monoiodotyrosine. Normally, neither monoiodotyrosine nor diiodotyrosine appears in the blood.

The generally accepted mode of formation of thyroid hormone is by condensation of two iodotyrosine residues with the extrusion of an alanine group. A whole series of such iodothyronines could be formed – and are formed. Thyroxine (3,3', 5,5'—tetraiodothyronine) was the first to be prepared (*Kendall* 1915) and identified (*Harington* 1926). The demonstration of triiodothyronine in the thyroid by *Gross & Pitt-Rivers* (1952) was an important advance in modern thyroid research, being followed later by the studies of *Roche et al.* (1952), suggesting that other iodine-thyronine compounds, particularly 3,3'-diiodothyronine, may be present in the thyroid gland. There is still no agreement on the individual stages of the synthesis described. Nor is it known with certainty whether other hormones than thyroxine are secreted by the gland. Both triiodothyronine and 3,3'-diiodothyronine have been found in the peripheral blood but may be deiodination products of thyroxine. The iodinated tyrosines and thyronines are found in the gland in the form of peptide linkages as components of the thyroglobulin. Normally, or if the activity of the gland is increased, the thyroid cells may perhaps secrete the hormone direct into the blood. Thyroglobulin, of high molecular weight, is broken down by a protease to components small enough to traverse the epithelial cells and enter the blood. The protease is thought to be activated by thyrotropic hormone from the hypophysis. The mono- and diiodotyrosine released by the breakdown of the thyroglobulin, are broken up by a specific deiodinase (*Roche et al.* 1952), which removes the iodine from these two compounds.

The thyroxine contains the largest mass of the circulating iodide, the remainder being triiodothyronine and, possibly, 3,3'-diiodothyronine. The thyroxine in the blood is bound to a carrier protein, which has an electrophoretic mobility like α_2 -globulin. A small proportion of the thyroxine is bound to albumin. The triiodothyronine is found more loosely bound and more equally distributed among the various serum components. Thyroxine and triiodothyronine can be extracted from serum with acid butanol.

Protein-bound iodine in the serum is normally found in amounts of approximately 3.5–8 $\mu\text{g}\%$. As a rule, high values are found in hyperthyroidism, low values in hypothyroidism.

Normally, the thyroid gland secretes between 1 μg and 200 μg daily of hormonal iodine, and of this amount about 10 per cent is turned over in the tissues daily. This secretion and turnover in the tissues is increased in hyperthyroidism.

The amount of circulating thyroid hormone also seems to have an influence on the thyroid function (*Cortell & Rawson* 1944).

Finally it appears as if the amount of iodine in the thyroid gland has some significance for its activity (*Halmi 1954, Wahlberg 1955*). Information is still lacking on many of the factors and influences determining the function of the gland.

PREVIOUS STUDIES OF PATIENTS WITH HYPOTHYROIDISM AND GOITRE

These patients can be divided into two groups. In the one group the disease is the result of lack of iodine in the diet, while in the other group the disease is the result of disturbances in the hormone production of the thyroid gland following (congenital) enzyme defects or the ingestion of certain substances, such as thiouracil—and in certain cases both factors seem to be involved.

ENDEMIC CRETINISM

The classic example of hypothyroidism with goitre as a result of lack of iodine in the diet is "endemic cretinism". *Platter* in 1614 described most of the symptoms of the disease as they are now known; mental and physical retardation, deaf mutism and goitre in sections of the population, adults as well as children, in certain parts of the Alps and various other places. The disease is often of familial occurrence in these goitrogenic regions, and seems to become exacerbated on passage from one generation to another. This has been explained as a result of the iodine stock of the family being gradually used up. Possibly a more plausible explanation is that genetic factors play a part (*McCarrison 1917*). Consanguinity is often pronounced in these regions. A confirmation that the lack of iodine can cause a latent, genetic or primarily determined defect in the hormone production of the thyroid gland to become manifest is provided by the studies of *Costa et al. (1953)*. They found that in three out of ten cretins in Northern Italy there was an enzyme defect of the thyroid gland. As a rule, but not always, a goitre is found in endemic cretinism, often containing adenomas, cystic degeneration and fibrosis. In some cases the goitre is able to accumulate iodine and produce varying amounts of hormone. "Paradoxical" cases of hyperthyroidism have been described in cretins.

A more detailed study of endemic cretinism lies outside the scope of the present study. Reference should be made to a very detailed *W. H. O.* report giving the literature on endemic goitre, and in which endemic cretinism is discussed in detail (*Bull. Wld Hlth Org. 1958*).

The report mentioned provides a collected discussion of the conditions in various countries, including Denmark, where endemic goitre has been described by *Christensen (1926)*, *Dalsgaard-Nielsen (1933, 1940)* and *Rosenquist (1943)*.

ENZYME DEFECTS IN THE HORMONE PRODUCTION OF THE THYROID GLAND

Osler in 1897 drew attention to non-endemic cases of hypothyroidism with goitre, apparently without any lack of iodine in the diet, and often familial. A series of similar cases has been described since, but it was not until the use of isotope studies, in connection with chromatography etc., revealed a number of the defects in hormone synthesis and hormone secretion of the thyroid gland, that the study of these cases attracted any considerable attention. On the one hand, we are now better able to classify the individual cases and reveal sub-clinical conditions, thus improving the possibility of a genetic prophylaxis, and on the other hand the study of these rare cases has thrown new light on the normal thyroid function.

The various types of defects will be discussed in what follows, and a review will then be given of earlier cases, together with those collected by the present author.

Three different types of disturbance of hormone production in the thyroid gland have been described particularly, but there are presumably others.

The first type consists of a lack of ability to link iodide to protein. This condition was demonstrated by Stanbury & Hedge (1950) and Stanbury (1951), who found a strong uptake of I^{131} in the thyroid gland of four patients with hypothyroidism and goitre, in a sibship of seven, as well as in a fifth patient. However, the I^{131} could be rapidly removed from the gland by oral administration of potassium thiocyanate. This could not be done in those cases where the iodide was converted into organic compounds with tyrosine or thyronine. Later, Stanbury *et al.* (1955), by direct analysis of gland tissue from one of these patients, showed that the iodine was present exclusively in inorganic form. In this case, it appears that the oxidation of iodide to iodine could not take place on account of an absent oxygenase, so there could be no incorporation of iodine in tyrosines and thyronines, neither could the iodinated forms of these amino acids be demonstrated in the glandular tissue. The authors demonstrated the same defects in two patients treated with imidazole. Thiouracil compounds, used against hyperthyroidism, appear to block the system in a similar way. The parents of the four siblings were cousins. Similar defects have been described by Jackson (1954), Lelong *et al.* (1956), Schultz *et al.* (1957) and J. U. Gardner *et al.* (1959).

A second type of enzyme defect appears to prevent the iodothyronines from taking part in the various combinations described in the section on the normal function of the thyroid gland. Stanbury *et al.* (1955) studied one of two sisters with hypothyroidism and goitre. In this patient, only very small amounts of thyroxine could be demonstrated in the blood. Likewise, only quite small amounts of thyroxine could be demonstrated in goitre tissue re-

moved at operation, but on the other hand large amounts of monoiodotyrosine and diiodotyrosine were found. The non-coupling of iodotyrosines is presumably due to an enzyme defect. The reason for thyroxine being present in the blood could be that small amounts of thyroxine were formed from the large quantities of precursors to thyroxine found in the gland, and these small quantities passed rapidly into the blood, or that under these circumstances a non-enzymatic coupling took place, a phenomenon which has been demonstrated in vitro.

Lelong et al. (1956) have a somewhat similar case in their material, and *Werner et al.* (1957) have studied a patient with hypothyroidism, goitre and a high level of serum-bound iodine (25 $\mu\text{g}\%$) equally distributed between thyroxine, triiodothyronine, diiodothyronine and monoiodothyronine, and in whom there seems to be an enzyme defect in the coupling of the diiodothyronines. *J. U. Gardner et al.* (1959) have similar patients in their material.

A third type of defect is *lack of deiodinase*. Normally, a deiodinase (*Roche et al.* 1952) removes the iodine from the monoiodotyrosine and the diiodotyrosine, which are released when the thyroglobulin gives up thyroxine and triiodothyronine to the blood. In normal subjects the blood does not contain monoiodotyrosine and diiodotyrosine. Patients lacking deiodinase have a very high and steep uptake curve for I^{131} , which shows a sudden fall within 24 hours. Patients with a curve like this have been described by *McGirr and Hutchison* (1953) in four siblings with hypothyroidism and goitre who have been closely studied since 1951. They belong to a large family of tinkers in whom the genetic relationships could be established. Hereditary cases of Werdnig-Hoffmann's disease are present in the same family (*Hutchison & McGirr* 1956). The whole clan originates from a consanguineous marriage. The thyroid gland defect is inherited recessively, and hypothyroidism and goitre appear in the children when the gene is present in the homozygous form. In this family, heterozygous parents are not hypothyroid. (*McGirr et al.* 1956). In a Dutch family, in which a number of the members are hypothyroid with goitre and the same type of metabolic defect, *Stanbury et al.* (1956) have shown that there are healthy family members with goitre whose uptake resembles that of the hypothyroid types, but to a less pronounced degree, and who presumably are heterozygous. *McGirr & Hutchison* postulated that their patients had an enzyme defect, but were unable to demonstrate the exact nature of this at that time. *Stanbury et al.* in 1955 succeeded in demonstrating that these cases involved a lack of deiodinase, as large amounts of monoiodotyrosine and diiodotyrosine could be demonstrated both in the serum and the urine of these patients, but not in normal subjects. Further, intake of monoiodotyrosine and diiodotyrosine labelled with I^{131} resulted in their rapid excretion unchanged in the urine of these patients, while in normal subjects under similar circumstances, inorganic iodine is excreted. Finally, it could be shown following operation that goitrous

tissue from a patient such as this could not deiodinate diiodotyrosine, as is the case with normal gland tissue.

McGirr *et al.* (1956) later found similar conditions in their patient. Stanbury *et al.* (1956) have studied three patients of this type, two brothers and a girl aged 12 years, all with goitre, the girl and one boy being hypothyroid in addition. Hubble (1953), Andersen (1955), Bergstrand (1956) and Werner & Block (1957), among others, have reported patients with hypothyroidism, goitre and uptake curves of the same type.

AUTHOR'S STUDIES OF HYPOTHYROID CHILDREN
WITH GOITRE (GROUP III)

Of the total material of 56 hypothyroid patients, 18 (approximately one-third) are found in this group. This frequency is about 2-3 times as great as the frequency usually reported for corresponding series. However, this can hardly be taken to suggest the presence of endemic cretinism in the classic sense. Endemic cretinism from lack of iodine is probably non-existent in Denmark today, even though in certain cases local conditions might possibly provoke a latent tendency.

Distribution of patients according to place of residence

The birth places of the patients are given below. The majority remained there for only a brief period, and now live in Copenhagen, where there is no endemic lack of iodine.

In the case of the patients born or living outside Copenhagen, enquiries were made as to the occurrence of endemic cretinism at these places, and in no case was it shown to be likely.

Copenhagen	7 patients
Scattered throughout Zealand	4 -
Scattered throughout Jutland	4 -
Island of Bornholm	1 -
Canada	1 -
Norway	1 -

The explanation for the unusually large number of patients in this group is, presumably, that the material is a selected one, in the sense that colleagues and institutions, for example the State School for the Deaf, were kind enough to send children in this category to the author. Furthermore, a number of these children presented their symptoms quite late, in addition deviating somewhat from the picture of classic congenital athyrosis, so in contrast to cases of the latter were referred for more special examination. In a number of these children, the goitre was not noticed before admission. Children such as these

can easily be classed in other groups depending on the limits used in defining the term goitre. Finally, a number of goitres in hypothyroid children on thyroid treatment were not noticed until treatment was withdrawn, and also for this kind of patient their placing in a group can be to some extent a matter of arbitrary choice.

For various reasons, to be mentioned in what follows, it is important that the diagnosis in these patients should be as exact as possible, both to clarify the whole clinical picture of hypothyroidism and for the sake of the patients themselves and their family.

CHARACTERISTICS OF GROUP III

Comparing this group as a whole (table XI) with Group I (table IV) and Group II (table VIII), various features are immediately obvious.

- (1) *Sex distribution*: there are almost equal numbers of boys (10) and girls (8), which corresponds to the finding of *Lelong et al.* (1956)) in an extensive review of their own and previously described cases. The sex distribution in the other groups is shown on page 56.
- (2) *The birth-order of the children* in this group showed 9 first-born out of a total of 20 children. This proportion, lower than that in Groups I and II (p. 44, 54), was to be expected, as a proportion of the patients are siblings, as opposed to the position in the other groups.
- (3) *High frequency of thyroid diseases in the family* (about 50 per cent of the cases). This agrees with what is usually quoted for this type of disease.
- (4) *High frequency of deafness (deaf-mutism)*, approximately one-third, which as far as the author is aware is much more than in any similar material.
- (5) *The relatively late time of manifestation*, and consequently the better mental prognosis. Two patients were diagnosed as having the disease before the age of one year, 9 between one and seven years and 7 patients later. The Group resembles Group II and differs from Group I in this respect (see fig. 6).

Table XI.

Group III: hypothyroid patients with goitre.
Cases no. 39-56

Case no.	Sex	B. weight, g B. length, cm	Symptoms first observed	Age at diag. and treatment	Treatment		Result		Heredity	Hearing
					duration	u. per day	phys.	mental		
39	M	3400/ 3000/	2-3 mth.	3 mth.	12 yr.	100-200 insuff.	R	R	pos.	deaf
40	F	4000/52	4-6 mth.	7 mth.	2 1/2 yr.	150-200	N	N	"	normal
41	F	4000/52	1-1 1/2 yr.	1 3/4 yr.	2 yr.	200-300	N	N	"	deaf
42	F	4500/57	6 mth.	1 10/12 yr.	7 yr.	100-200	N	N	"	"
43	M	3000/51	6 mth.	2 yr.	9 yr.	100-500	N	R	neg.	normal
44	M	3750/53	9-10 mth.	2 1/2 yr.	3 1/2 yr.	200-400	N	R/N	"	"
45	F	4000/53	1 1/2 yr.	2 1/2 yr.	0		R	R	"	"
46	M	4100/53	1 yr.	2 1/2 yr.	1 1/4 yr.	200	N	I.Q. = 73	"	"
47	F	3600/53	6 mth.	2 1/2 yr.	1 1/2 yr.	200 insuff.	R	R	"	"
48	F	3500/	2 yr.	3 yr.	13 yr.	100-200 insuff.	R	R	"	"
49	F	2750/51	1-1 1/2 yr.	3 yr.	4 1/4 yr.	175	N	N	"	"
50	M	3600/53	3-5 yr.	7 yr.	7 yr.	200-400	N	N	"	hearing impaired
51	M	3150/54	6-7 yr.	9 1/2 yr.	2 yr.	200	N	N	pos.	deaf
52	M	4200/57	10 yr.	10 yr.	1 1/2 yr.	200	N	N	"	normal
53	M	4000/	3 yr.	11 1/2 yr.	6 1/2 yr.	200-400	N	R	neg.	"
54	M	2500/52	11 yr.	12 1/2 yr.	0 yr.		R	N	pos.	deaf
55	M		12 yr.	14 yr.	0 yr.		R	N	"	normal
56	F	3000/	10-11 yr.	16 yr.	4 yr.	200-400	N	N	neg.	"

Fig. 6. Age at the time of diagnosis for patients in Group I, II and III.

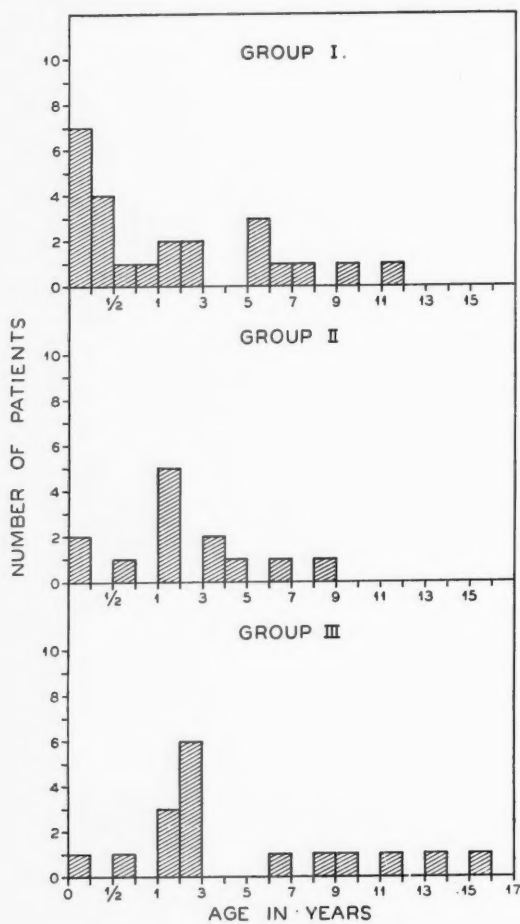


Fig. 6.

Group I: aplasia and hypoplasia of the thyroid gland.

Group II: sublingual, ectopic thyroid tissue.

Group III: hypothyroidism with goitre.

DEAFNESS IN PATIENTS IN GROUP III

As mentioned, there are surprisingly many deaf mute patients in Group III, both by comparison with Groups I and II and with the reports in the literature. Deaf-mutism is a characteristic sign in many patients with severe endemic cretinism.

The *W.H.O.* report (1958) on endemic goitre, mentioned earlier, gives a review of deaf-mutism in patients with endemic cretinism.

From this, it appears that in Switzerland, for example, 0.12 per cent of the population are deaf-mutes.

In about 40 per cent of these cases the condition is hereditary, in a number of the remainder it appears in cretins, while in others it is acquired or congenital. It is shown that deaf-mutism is inherited as a recessive characteristic, and that the hereditary factor can lie hidden for many generations. From these and similar considerations, it seems to be doubtful whether deaf-mutism in the children of cretins can be considered as a direct consequence of the disease. A number of studies have been made on the association between deaf-mutism and hypothyroidism. *Poulsen*, in his thesis on the influence of myxoedematous connective tissue changes on the function of the labyrinth (1959), has collected the literature on this subject, to which reference may be made.

Children with hypothyroidism and deaf-mutism seem to be infrequently described in the literature. In Denmark, *Vesterdal* (1957) has presented two siblings with goitre, hypothyroidism and deafness. During the subsequent discussion of the cases the present author pointed out that one of the causes of deafness in hypothyroid children might be changes in the mucopolysaccharides of the inner ear in analogy with what is found for the teeth and skin (page 103). *Poulsen's* experimental studies support this conjecture.

Thanks to the collaboration of doctors at the State schools for deaf children and children with severely impaired hearing, and also from other sources, the present author has been able for some years to study a number of children with hypothyroidism and deafness. In addition, among other of our hypothyroid patients, various types of hearing impairment have been demonstrated as a more accidental finding.

Considering these patients as a group, various reasons for their deafness would seem possible.

Of the two siblings, cases no. 42 and 54, both deaf from birth, and with a euthyroid mother without goitre and with normal hearing, the one (no. 42) was severely hypothyroid early in childhood, while the other (no. 54) did not show symptoms of hypothyroidism until the age of 10 years, and then showed only slight signs of hypothyroidism.

Hypothyroidism as a cause of deafness in these two children can be excluded in no. 54. On the other hand, the possibility cannot be excluded that this may be a case of "linked" hereditary defects, even though the nearest family members apparently do not include similar cases. Quite another cause seems possible, as during the first half of both pregnancies the mother received vigorous treatment with sulphonamides (type?) for cystopyelitis. As it seems to be confirmed that sulphonamide treatment during pregnancy can produce kernicterus in the offspring, it is not unlikely that deafness can also be a sequela

Table XII.

Patients with hypothyroidism and goitre.

Cases no. 39-53

Case no.	Sex	Hereditary	Hearing	Age at diag.	Goitre			P.B. Lug. % (3.1-6.1)
					Noticed	Type	Reaction to treatment	
39	M	Mother's sister has goitre	deaf	3 mth.	?	Small, soft, diffuse		2.4
40	F	Mother has goitre, not treated	normal	7 mth.	At birth	Small, soft		2.0
41	F	Father's mother had opn. for "goitre".	deaf and dumb	1 3/4 yr.	At diag.	Small, soft	Disappeared after 6 mth.	0.7
42	F	Older brother (case no. 54), has same disease	deaf and dumb	1 10/12 yr.	9 yr.	Small, soft, diffuse (patient is under treatment)	?	6 (during tr.)
43	M	negative	normal	2 yr.	?	Rather large, diffuse and soft	?	0.5
44	M	"	"	2 2/12 yr.	At diag.	Small, diffuse, very soft	Disappeared after 3 mth.	2.5-3.7
45	F	"	"	2 2/12 yr.	At birth	Large, diffuse, soft	Disappeared after 2 mth.	4.5
46	M	"	"	2 2/12 yr.	At diag.	Small, soft	Disappeared after 3 mth.	6.0
47	F	"	"	2 2/12 yr.	At diag.	Small, soft		(during tr.)
48	F	"	"	3 yr.		Large, diffuse, soft		0.4
49	F	"	"	3 yr.	At diag.	Large, diffuse, soft	Decreasing	1.4
50	M	"	impaired	7 yr.	2 yr.	Rather small, diffuse	Decreasing	0.4
51	M	Mother's sister + her two children have goitres. No deafness or dumbness in family	deaf and dumb	9 2/12 yr.	At birth	Rather large, a few nodules. Thyroidectomy at 5 yrs., recurred 9 1/4 yr.		0.9
52	M	Mother had opn. for goitre at 16 yr.	normal	10 yr.	5 yr.	Large, rather soft, a few nodules	Decreasing ?	2.7
53	M	negative	normal	11 7/12 yr.	At diag.	Small, fibrous, diffuse	Disappeared after 6 mth.	

Table XII contd.
Patients with hypothyroidism and goitre.
Cases no. 54-56

Case no.	Sex	Heredity	Hearing	Age at diag.	Goitre			P.B.I. $\mu\text{g}\%$ (3.1-6.1)
					Noticed	Type	Reaction to treatment	
54	M	See case no. 42	deaf and dumb	12 ⁶ / ₁₂ yr.	6 yr.	Rather large, soft with a few nodules		5.1
55	M	Mother's mother has goitre, Graves' disease ? Mother's two brothers have impaired hearing Brother to no. 55	normal	14 yr.	At birth	Large, diffuse. Opn. at 12 yr., recurred 14 yr.	Decreasing	1.7
55A	M		"	5 ⁸ / ₁₂ yr.		Palpable but not really enlarged		0.8
55B	F	Sister to no. 55	"	7 yr.		Palpable but not really enlarged		3.8
56	F	negative	"	16 yr.	At diag.	Small, soft, diffuse	Decreasing after 3 mth.	

to this. This question cannot be discussed further without a closer examination of the circumstances obtaining in these children. However, the cases throw light on a number of the possibilities requiring investigation.

In other cases (nos. 39, 51), the deafness seems to be explained as a result of post-natal otitis or possibly, in the severe cases of hypothyroidism, as a direct result of the accumulation of mucopolysaccharides in the inner ear. Our data are still too scanty to permit analysis of these relationships in further detail here.

FURTHER STUDIES OF CHILDREN IN GROUP III

Dental studies of Group III were made in about half the cases and show the same results as in the other groups, which was to be expected, as in all hypothyroid patients it is the lack of hormone which determines the clinical picture, no matter the reason for the lack.

The serum cholesterol values in this group show nothing of special interest.

Protein-bound iodine is shown in table XII. Where nothing is stated, the values are effective for patients in the untreated state or after 3-6 weeks' withdrawal of thyroxine treatment. As the table shows, the majority of the values are under the normal limit, though with two exceptions, cases no. 46 and 54, thus agreeing with the findings of others, see page 62.

Histological examination of hypothyroid goitres

The following reports are available for those patients in whom thyroidec-tomy was performed (cases no. 51, 52 and 55).

Case no 51

First operation: macroscopic examination: Two slightly unequal pieces of tissue without nodules, haemorrhage, cysts or calcification, about $\frac{3}{4}$ the size of a hen's egg, elongated, rounded, pointed at the ends, flattened, not quite 2 cm thick, solid, greyish, firmly elastic, non-brittle, lobulated and of uniform structure. The tissue pieces weigh 18 and 24 g respectively when fixed.

Microscopic examination. Both thyroid fragments show the same appearance, being finely lobulated, poor in stroma, of uniform structure. The numerous thyroid follicles are densely packed throughout, average to large in size, round, elongated, partly tubular but not trabecular, with a tendency at times to branching of the tubules. The epithelial cells are quite large, cubic, clear: the nuclei show a tendency to some enlargement, there are no mitoses. The lumen of the follicles is most often empty, more rarely a weakly stained colloid is seen with small peripheral vacuoles. There are no circumscribed nodules or cysts. There is no necrosis, haemorrhage, round cell infiltration,

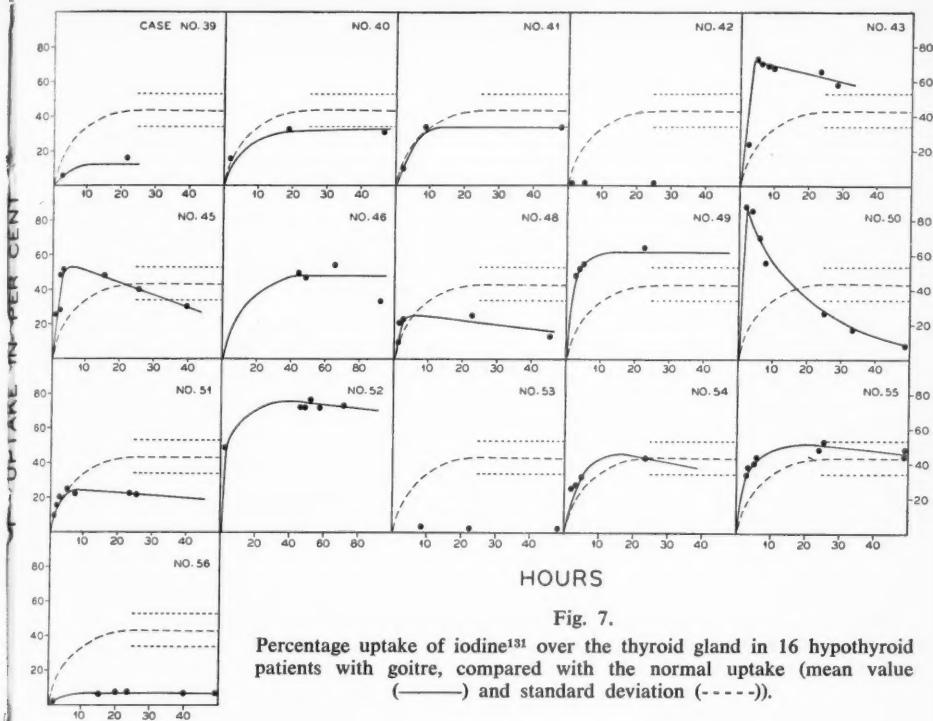


Fig. 7.
Percentage uptake of iodine¹³¹ over the thyroid gland in 16 hypothyroid patients with goitre, compared with the normal uptake (mean value (—) and standard deviation (----)).

scarring or calcification. There is no parathyroid tissue in the sections examined. The follicular epithelium is nowhere of high cylindrical type, nor are the follicles pronouncedly polymorphic with strip-like projections into the lumen as in Graves' disease, just as the lymph follicle formation generally occurring in this disease is absent.

Microscopic diagnosis: struma diffusa parenchymatosa micro-follicularis et tubularis. (Signed) Petri.

Second operation: macroscopic examination: — Two pieces of tissue, approximately walnut-size, elongated, rounded and lobulated, slightly tattered, consisting of a large, round, pale, whitish, solid, uniform, softly elastic, brittle, nodular, non-colloid-containing portion with adjacent fibrous tissue parts, in which are seen brownish, dense, small-lobulated, almost tough, non-colloid-containing thyroid tissue parts. The tissue was then fixed.

Microscopic examination. Both thyroid tissue portions contain round nodules, a good hazelnut in size, rich in cells, dense, of uniform structure, and consisting of numerous epithelial cells with a densely packed tubular, trabecular

and particularly micro-follicular arrangement; these are of average size, rounded-cubic, clear, uniform, with no difference in nuclear size and without mitosis, arranged in one layer. A weak-staining colloid is seen in the majority of the small follicles. The inter-follicular stroma is very scantily represented, moderately vascular, slightly oedematous or mucoid in places. The nodules are delimited by a fibrous connective tissue proliferation of a scar-like nature and average thickness, disappearing peripherally into a striated musculature and containing small strands and islands of atrophic thyroid tissue. In supplementary sections a small nodule is also seen consisting of numerous densely packed, lobularly arranged thyroid follicles, sometimes smaller, sometimes larger, most often of irregular shape, with small striplike projections. The epithelium is clear, flat cylindrical, single-layered, and the cells are of good average size. The follicles contain a weakly-stained non-vacuolated colloid. The structure of the thyroid section last described recalls the appearance of Graves' disease.

There are no demonstrable parathyroid parts; a small half-hemp seed-sized nodular portion lying superficially in both thyroid tissue pieces, although resembling parathyroid gland, nevertheless also shows resemblance to the adenomas described above in the thyroid gland itself.

Microscopic diagnosis: adenomata gl. thyreoidea parenchymatosa micro-follicularis et tubularis et trabecularis. Strongly fibrous thyroid tissue with scar formation, almost nodular: atrophic follicles, follicles resembling Graves' disease. (Signed) Petri.

Case no. 52:

Colloidal goitre.

Case no. 55:

17 g of thyroid tissue removed on the left side and 47 g on the right side.

Microscopic diagnosis: nodular goitre, with pronounced adenomatous features, fibrosis and cyst formation in parts with fresh and older haemorrhage of the type seen in endemic goitre with slight features of thyrotoxic activity.

Previous descriptions of the histological findings are available in a number of the studies mentioned (see page 61). *Lelong et al.* in 1956 collected 18 such descriptions from the literature, including their own cases. The material originates from thyroidectomies or thyroid biopsies, and in general the findings are fairly uniform: often quite pronounced polymorphy with nodular portions, showing signs of strong activity, now and again of adenocarcinomatous appearance. However, cancer is never observed. Other parts in turn are follicular, with greater or lesser colloid content. *Werner et al.* (1957) give a description of a case where particularly large distorted follicles dominate at the expense

of the adenomatous portions. Our patients, however, particularly cases no. 51 and 55, seem to show good agreement with these descriptions, whereas case no. 57 shows a more uniform follicular structure.

I¹³¹ uptake in patients in Group III. This is shown in the curves of fig. 7 for the individual patients, with the exception of cases no. 44 and 47, in whom only one measurement was made after 24 hours.

Under the circumstances at the time, it was unfortunately impossible for the present author to carry out fractionation and determination of the individual iodinated amino acids and hormone fractions, with the intention of arriving at a fundamental elucidation of the enzyme defects. Administration of potassium thiocyanate was tried in only two cases, without any effect. If this or perchlorate had been administered consistently, there is no doubt that more would have been found out about the nature of the enzyme defects.

The shapes of the curves in fig. 7 are quite uniform, apart from case no. 50, the appearance of which strongly recalls the picture in patients with lack of dehalogenase (see page 62); a similar curve shape is reported in patients with Hashimoto's disease. Antigen studies could have distinguished the two types.

The other curves deviate from each other more in level than in shape, presumably representing various defects and various degrees of defect.

Lelong et al. (1956) found a similar state of affairs in their review of all cases of this type reported, a total of 40, including their own material.

It is difficult to compare the uptake percentages quoted by the various authors, as their normal values vary very considerably, but an estimate showed that after 48 hours the values in 31 patients were above normal, within the normal range in 6 patients and lower than normal in 3 patients. However, values measured for example after 24 or 48 hours are in themselves of no particular use. As the curves show (fig. 7), if one were satisfied with a *single measurement* after 24 or 48 hours, values could be obtained in various patients which were low, normal or too high. Compared only with normal values, these patients would be diagnosed as having hypo- or hyperthyroidism. One of the reasons why measurements with I¹³¹ have become discredited in some quarters is undoubtedly that too few measurements have been made. If for example the curve for case no. 50 is examined (fig. 7), the 24 hour (and 48 hour) measurements show commonplace "hypoplasia values", and give no indication of the far more dramatic course during the period 0-24 hours.

From the data available, it cannot be decided whether the patients in Group III all have enzyme defects or whether they represent various diseases of completely different pathogenesis.

A number of the patients in Group III should undoubtedly be placed in the group with enzyme defects. Even though these patients are not the most

numerous in the entire material, they are by no means altogether uncommon. A thoroughgoing investigation by methods other than those available to the present author would be of the greatest interest, not only to clarify the pathological and normal processes of hormone production, but also to elucidate the *heredity* and thereby the *genetic prophylaxis*. For the present, the last two aspects are the points at which a particular effort could be made to combat the disease, so long as we do not know the etiology of aplasia and hypoplasia.

Chapter VI

RARE FORMS OF HYPOTHYROIDISM

HYPOTHYROIDISM RESULTING FROM EXTRA-THYROIDAL ENZYME DEFECT

Hutchison et al. (1957) have reported such a case, as far as the present author is aware the only one so far known. The patient was a 4-year-old hypothyroid girl who did not react to the usual treatment with desiccated thyroid. On the other hand a completely satisfactory result was obtained with triiodothyronine. *Hutchison et al.* mention the possibility that the thyroxine in the tissues of this child is not deiodinated to triiodothyronine by a special enzyme, as otherwise presumably takes place.

DISEASE OF THE THYROID GLAND RESULTING FROM AUTO-IMMUNISATION

The study of *Hashimoto's* lymphatic struma (1912) has opened up new perspectives for our understanding of the mode of origin of this and perhaps a series of other diseases. In the beginning of the fifties, several investigators found raised levels of gamma globulins in serum from patients with *Hashimoto's* disease. The association between the gamma globulins as the carriers of antibodies, and the presence of lymphoid tissue and plasma cells in *Hashimoto's* struma, led to the assumption that the changes in the thyroid gland in this disease were the sequelae of an antibody-antigen reaction, taking place in the thyroid tissue and in the surrounding lymph nodes. *Roitt & Doniach* and colleagues (1956-57) have shown in a series of studies that sera from the majority of these patients contains thyroxine-specific auto-antibodies, which can be determined by a precipitation test. Later, other methods were described for demonstrating the antibodies, such as the complement fixation reaction, etc. The antigen is considered to be thyroglobulin, which escapes from the thyroid gland under certain circumstances and causes antibody formation, for example in the surrounding lymphoid tissue. The antibodies then react with the thyroglobulin in the thyroid gland, producing a lymphoid reaction here, with damage to the thyroid tissue, so that more thyroglobulin is allowed to escape from the

thyroid gland, and so on, a vicious circle being established. *White* (1957), using fluorescein-marked Hashimoto antibody, was able to demonstrate its occurrence in the epithelium of the thyroid and in the surrounding lymph nodes.

One consequence of this discovery has been that most cases of Hashimoto's disease are now successfully treated by means of thyroxine in such large doses that the hormone production of the gland is stopped.

By far the majority of cases of Hashimoto's struma occur in middle-aged women. However, the disease has also been described in children. *Stadtland et al.* (1951) thus described the disease in two girls aged 10-14 years, the latter having had goitre from the age of 6 years.

The most frequent symptoms are goitre of varying size and consistency, a feeling of fullness, and pain in the throat. *Beare et al.* (1958), in a series of 33 patients, found hypothyroid symptoms of mainly slight degree in one-third of the patients.

Hashimoto's antigen has also been demonstrated in patients with hypothyroidism without goitre, as well as in a number of patients with hyperthyroidism, possibly the result of strong stimulation of the gland. I^{131} uptake is high, with a sudden fall, the explanation being that these patients have only a small iodine reservoir in the thyroid gland.

Beierwaltes et al. (1959) with the help of precipitin tests on the mothers of hypothyroid children, have shown recently that the transfer of thyroid antibodies from the mother to the foetus hardly plays any great role as a cause of congenital hypothyroidism.

Chapter VII

GOITRE IN EUTHYROID PATIENTS (»SIMPLE GOITRE«)

PREVIOUS STUDIES

Even though this form of the disease lies outside the scope of this study, certain of its features will be mentioned. On the one hand, in the patient material tested with I^{131} for suspected hypo- or hyperthyroidism, there have been a number of patients with goitre who were found to be euthyroid, either by other tests or by the subsequent course; on the other hand, some of the simple goitres seem to present a condition closely linking them with goitrous hypothyroidism. On the whole, it seems that the simple goitres conceal more of interest for our understanding of normal and pathological thyroid function than has at times been realised.

The various forms of goitre in childhood have been described in detail, e. g. in *Wilkins' handbook* (1957), which also lists a comprehensive literature on the subject. Congenital goitres have been described by *Bongiovanni et al.* (1956), for example, where a review of previously described cases is also found.

The well-known causes of simple goitre, for example the intake of goitrogenic substances, thiouracil, thiocyanate, certain sulphonamides, cabbage etc., either by the patients themselves or by the mother during pregnancy, appear to play a numerically minor role. Endemic lack of iodine is rare, at least here in Denmark. Nor are inflammatory or auto-immunizing processes common, such as Hashimoto's struma and Riedel's struma. According to Wilkins, primary or metastatic neoplasms occur in about 2 per cent of *all* patients with thyroid disease. In a material consisting of 430 thyroid cancers, *Duffey & Fitzgerald* (1950) found 28 in children under the age of 16 years. Goitres occurring especially in young girls around puberty play a numerically greater role. *However, the cause of most "simple goitres" is not known.*

It is a well-known fact, and often described both abroad and in Denmark, that goitres occur in certain families, with several or all of the siblings having the disease. On page 61 a corresponding picture is described in patients with hypothyroidism and goitre as a result of a congenital defect of hormone synthesis. In 1953, *Greer & Astwood* suggested that a similar mechanism might

be the cause of a number of simple goitres. These could be considered as subclinical cases of hypothyroidism, either compensated throughout life, or until the demand imposed became greater than the hypertrophic thyroid could meet, for example when the children grew up. They drew their conclusion, for one thing, from the good results achieved by treating patients with simple goitre with thyroxine. This treatment, previously employed but later on less popular, has once again come to the fore. In particular it seems to have a good effect on diffuse goitres in young subjects, whereas the nodular forms do not react so well, or do not react at all. *Greer & Astwood* found that patients with a high uptake curve over the thyroid gland following I^{131} intake, reacted particularly well to the treatment.

Subsequently *Sampson et al.* (1956) showed that 1-triiodothyronine has a similar and in certain cases better effect.

Clayton et al. (1958) showed that in certain families there are children with simple goitre as a result of impaired ability of the thyroid gland to couple iodide to the thyroid hormone, demonstrating this condition in several members of the same sibship.

It is not known how often this kind of defect is the cause of simple goitre. It seems reasonable, for one thing on the basis of our information of enzyme defects in children with hypothyroidism, to suppose that various types and degrees of defects in enzyme synthesis may be involved in patients with simple goitre. These could be revealed with the aid of the methods mentioned in the section on enzyme defects in hypothyroidism. In this way there would be more clarity as to the genetic relationships, and possibly an indication as to which forms might proceed to hypothyroidism. There would thus be improved possibilities for the introduction of adequate therapy in due time. Similar considerations could apply to hyperthyroidism. The relationship between simple goitre and hypothyroidism is far from clarified.

AUTHOR'S STUDIES

Table XIII and the curves of fig. 8 provide a review of the euthyroid patients with goitre, on whom I^{131} studies were made. Unfortunately, tests were not made with potassium thiocyanate, which is an omission, nor were attempts made to study the I^{131} turnover either chromatographically or in another way, as apparatus sensitive enough for the doses with which the present author was willing to work, was not available.

It appears from the various data that in a large number of children there is a family history of thyroid disease, particularly on the mother's side. In this and in a number of similar series, the figure found is presumably not a true expression of the frequency of familial occurrence. For example, mothers

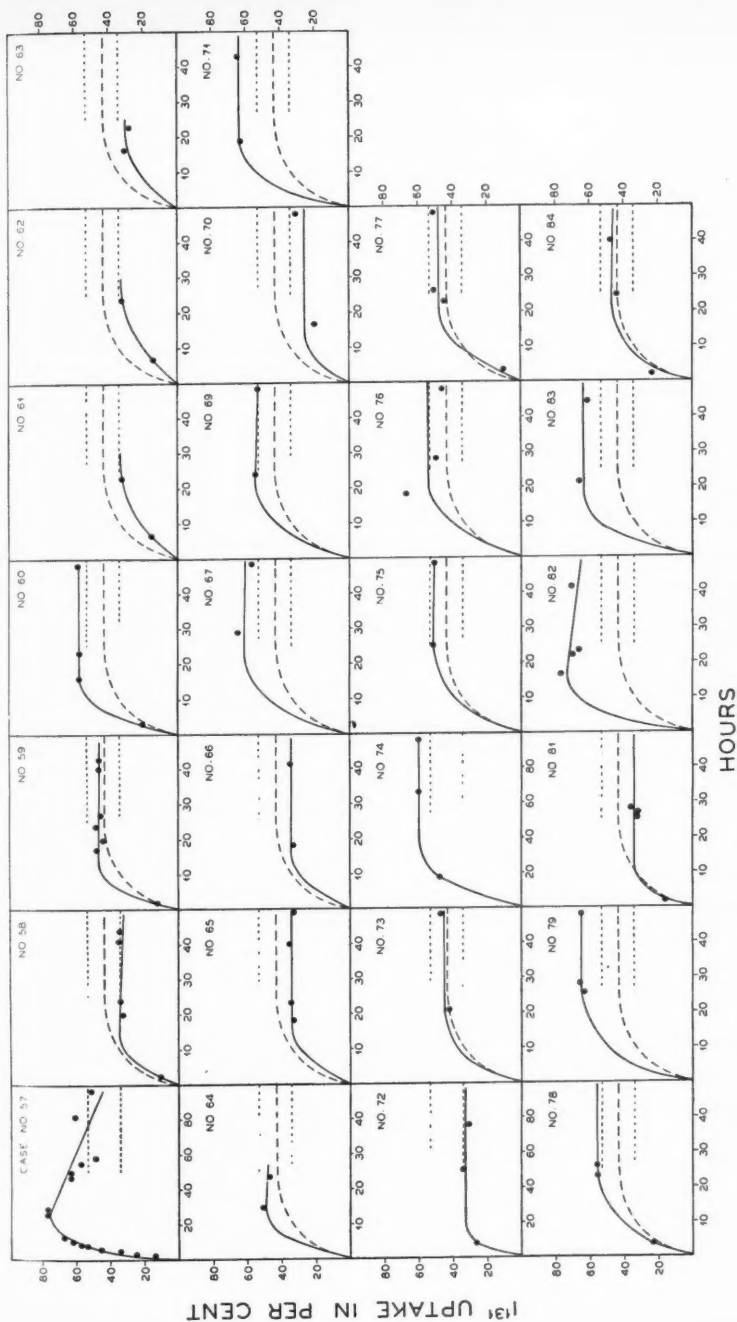


Fig. 8.

Percentage uptake of iodine¹³¹ over the thyroid gland in 26 euthyroid patients with goitre, compared with the normal uptake (mean value (—) and standard deviation (----)).

Table XIII.
Euthyroid patients with goitre.
Cases no. 57-74.

Case no.	Case record no.	Sex	Age	Heridity	Goitre			P.B.L. $\mu\text{g}\%$ (3.1-6.1)
					Noticed	Size	Type	
57	908/55	M	8 yr.	Negative	At diag.	Small	Soft, diffuse	-
58	1459/54	M	9 ¹⁰ / ₁₂ yr.	Mother has goitre, Graves' disease?	"	"	"	-
59	1295/54	F	8 ⁸ / ₁₂ yr.	negative	"	"	"	-
60	632/55	F	14 yr.	negative	10 yr.	Med.	"	-
61	735/55	M	11 ⁸ / ₁₂ yr.	Mother operated on for Graves' disease	11 yr.	Small	"	-
62	642/55	F	11 ⁹ / ₁₂ yr.	Mother operated on for Graves' disease. Father's mother died from Graves' disease	At diag.	"	"	-
63	714/55	F	1 ¹ / ₂ yr.	negative	At birth	"	"	6.2
64	760/55	M	9 ⁷ / ₁₂ yr.	negative	"	"	"	4.0
65	1113/55	F	14 ¹ / ₂ yr.	Mother has non-toxic goitre	11 yr.	"	"	-
66	1308/55	M	9 ¹⁰ / ₁₂ yr.	negative	At diag.	"	"	-
67	1446/55	M	11 yr.	negative	"	"	"	-
68	1591/55	F	13 ³ / ₄ yr.	negative	"	"	"	-
69	264/57	M	10 ¹ / ₁₂ yr.	Mother operated on for non-toxic goitre	10 yr.	Med.	"	6.1
70	300/56	F	5 ⁸ / ₁₂ yr.	Mother's sister's son has goitre	At birth	"	"	2.4-4.0
71	1181/56	M	12 ² / ₁₂ yr.	Mother had goitre in pre-puberty. Remitted spontaneously	"	"	"	-
72	215/57	M	4 ³ / ₁₂ yr.	Mother's mother and sister have Graves' disease	4 yr.	"	"	6.6
73	260/57	F	6 ⁸ / ₁₂ yr.	Mother has goitre	7 yr.	"	"	-
74	368/57	F	12 ⁷ / ₁₂ yr.	Father's father operated on for Graves' disease	-	"	"	3.5

Table XIII contd.
Euthyroid patients with goitre.
Cases no. 75-84.

Case no.	Case record no.	Sex	Age	Heredity	Goitre			P.B.I., $\mu\text{g}\%$ (3.1-6.1)
					Noticed	Size	Type	
75	695/57	F	12 yr.	Mother operated on for Graves' disease	10 yr.	Med.	Nodular	5.5
76	1507/57	M	13 ¹⁰ / ₁₂ yr.	Mother operated on for Graves' disease	-	Small	Soft, diffuse	3.5
77	1591/57	F	15 ⁹ / ₁₂ yr.	Father's brother has Graves' disease?	7 yr.	Med.	"	4.9
78	1505/57	F	12 ⁴ / ₁₂ yr.	Mother has goitre, on thyroid therapy	At diag.	Small	"	7.3-7.1
79	1606/57	M	7 yr.	negative	"	"	"	5.0
80	463/58	F	7 ¹ / ₁₂ yr.	Mother's sister had goitre, disappeared spontaneously	"	"	"	-
81	692/59	F	14 ¹ / ₁₂ yr.	Mother's mother and two of her sisters have goitres	12 yr.	Large	Soft with a few nodules	2.0
82	1352/59	F	7 ¹ / ₄ yr.	Mother's mother and sister have Graves' disease?	At birth	Med.	Soft, diffuse	3.8
83	153/59	M	12 ⁴ / ₁₂ yr.	Mother and a younger brother have goitres	?	"	"	5.9
84	462/59	F	6 ¹ / ₂ yr.		?	Small	"	7.7-7.3

who have had a thyroid disease themselves will on the whole be more on the look-out for the occurrence of goitre in their children, and will be more likely to have them examined. On the other hand, the present material has not been prepared with particular attention to the genetic circumstances, and it is obvious that meticulous questioning would bring to light still more familial cases. The curves for the uptake of I^{131} have on the whole the same shape. On the other hand, the level reached after 24 hours varies, presumably expressing varying functional conditions in the different patients. There is no direct association between the age of the patients, the size of the goitre or its duration, and the shape of the curves. It would seem that the patients with too low P. B. I., cases no. 70 and 81, have low uptake curves. Otherwise there is no direct association between the curves and the P. B. I., *just as P. B. I. values are found both above and below normal.*

No definite conclusion can be drawn from the present data, nor, as mentioned, were the investigations intended for the study of simple goitre. There are, however, only few studies of I^{131} in this type of patient, and the intention is to follow up these children and see how they develop. The results now recorded may serve later as a basis for studying the prognostic and genetic aspects of the disease.

Chapter VIII

X-RAY CHANGES IN CHILDREN WITH HYPOTHYROIDISM

PREVIOUS STUDIES

The normal function of the thyroid gland is strongly to accelerate the growth and development of the skeleton. Thus, when a child is affected by hypothyroidism, far more serious changes will be caused, and more important for the diagnosis and dating of the onset of the disease, than in an adult patient.

Although the disease is generalised in its nature and must therefore be assumed to affect all the bones, which it can also do, the *changes in the epiphyses of the bones of the extremities* are those which have attracted particular attention, and on which a comprehensive literature is available.

As early as the beginning of the present century, the duration and degree of severity of the disease was determined from the extent of retardation of the bone centres—especially in the wrist (see page 13). *Langhans* in 1897, in an autopsy report, describes the *changes in the epiphysial-diaphysial cartilage* in cretins. Scattered reports on X-ray and pathological changes in various epiphyses appeared later particularly of the hip joints of patients with endemic cretinism.

Reilly & Smyth in 1937 described what they called "*cretinoid epiphysial dysgenesis*" in five severe cases of hypothyroidism aged 5–15 years, a designation still employed. The changes found appeared as scattered centres of ossification in the epiphysial cartilage, usually bilateral and most pronounced in the epiphyses of the long bones. The authors believed that not all patients with hypothyroidism developed these changes. The patients were treated with various forms of medication, including thyroxine, regarded as being the most effective.

It was not until *Wilkins'* great study in 1941 that epiphysial dysgeneses were accorded the importance in the diagnosis and understanding of hypothyroidism which they still possess. *Wilkins* made it clear that the changes were of a highly specific, almost pathognomonic nature, that they affected the epiphyses whose development was proceeding at the time in question, or the new ones which appeared subsequent to treatment, that the later epiphysial

development under adequate therapy took place normally, but that fresh dysgeneses could arise in centres which were in the course of development during periods when treatment was neglected. *Wilkins* considered that hypothyroidism inhibits normal ossification, and that the calcification processes which start functioning with some years' delay in the untreated cases do not take place, as normally, from a central nucleus, but from scattered foci in the epiphysial cartilage. The ossification is strongly accelerated during treatment. The scattered centres grow, until they become larger and larger grains, appearing as "stippled epiphyses" on the X-rays. New centres appear, and finally a more or less normally developed epiphysis is produced depending for one thing on whether it has been subjected to secondary deformation by load, as can be seen for example in the head of the femur.

If hypothyroidism occurs later on in childhood, it affects only those epiphyses which calcify after this time, for example the patella and the apophysis of the calcaneus. These centres, however, may normally have a somewhat stippled appearance at this age, so the value of these findings must be judged with care and after taking repeated X-ray pictures during treatment.

The peripheral dysgeneses are however so well known and well described that they will not be discussed further here.

Tables of the development and appearance of the epiphyses at various ages are given in the handbooks and X-ray atlases (*Wilkins, Caffey etc.*), whereby the bone age can be determined. A delay in the bone development is in itself no proof of hypothyroidism, but on the contrary, normal bone development tells strongly against prolonged hypothyroidism, in fact almost excludes this possibility. As the epiphysial dysgeneses affect the various epiphyses to different degrees, depending on the age of the patient and the duration of the disease, exposures showing the epiphyses in "one half of the skeleton" are usually much more useful than merely an exposure of the wrist. Furthermore, bone maturation both in the untreated patient and during the first stages of treatment is often very irregular, with up to several years' difference in bone age at various points of the skeleton. A mean value must then be chosen, or the region specified which is being used, for example the hand, and *Greulich's* atlas or a similar standard reference employed.

In cases of doubt and at the first examination it is useful to take an X-ray picture of a skeletal segment as mentioned, and it is important to make a careful examination for dysgeneses, as the demonstration of these is far more significant for the diagnosis than the unspecific information on how many centres there are in relation to normal.

PRE-NATAL BONE DEVELOPMENT IN INFANTS WITH HYPOTHYROIDISM

The determination of the bone centre development in infants with hypothyroidism has a certain significance for whether intra-uterine hypothyroidism may have existed (see pages 45, 46, 47, 48, 54, 55).

Dorff, in 1934, was the first to demonstrate lack of development of the bone centres in the knee (distal femur centres and proximal tibia centres) in a 17-month-old twin with congenital hypothyroidism. The other twin was healthy and had a normal bone centre development. *Dorff* interpreted the finding as a sign of intrauterine hypothyroidism, and based on this, among other things, he suggested that the foetus depends on its own thyroid function, and that receipt of thyroid hormone from the mother via the placenta, or from the mother's milk after birth, is unlikely (see page 106).

Others (for example *Wilkins* 1957) have shown in hypothyroid children a corresponding lack of bone centres normally present at birth. This, in turn, raised the question: which bone centres are normally present at birth? According to *Christie's* study (1949), of 1112 newborn, *distal femur epiphyses occur in 100 per cent of newborn white boys and girls with a birth weight ≥ 3000 g.* In the weight group between 2500 and 3000 g the figures are 98 % and 85 % for boys and girls respectively, and in the group 2000–2500 g the figures are 91.7 % and 75 % respectively. As hypothyroid children who are diagnosed early are generally of normal weight or above (see page 47), and—as the mother herself often states—“late”, it seems reasonable to assume that absence of the lower femur centres represents a retarded “prenatal” bone development in these children. There is still no definite estimate of how many of these children with early manifest hypothyroidism lack this centre. Routine examination of the knee joint or of “one half of the skeleton”, instead of a wrist or ankle, could help to clarify this point.

In newborn white children the proximal tibia epiphysis is found in about 80 per cent of those weighing 3000 g and more, and in the same weight class the cuboid centre is found in about 40 per cent of the boys and 65 per cent of the girls.

In *Elgenmark's* (1946) study of the normal bone development in Swedish children, the distal femur centres are reported present at birth in 97 per cent of all newborn boys and in 95 per cent of all newborn girls. For the proximal tibia centres the figures are 96 per cent and 95 per cent respectively, and for the cuboid centre 93 per cent and 95 per cent respectively. As far as the present author can see, *Elgenmark* has made no classification according to birth weight, and none of the newborn were examined immediately after birth.

Differential diagnosis. From the point of view of differential diagnosis, localised osteochondritis, for example *Calvé-Legg-Perthes'* disease and various multiple epiphyseal degenerations, can be mistaken for hypothyroid changes,

but the bone centre development in these euthyroid conditions will be normal or only slightly retarded. Patients with such a degree of hypothyroid epiphysial dysgenesis as to suggest the diseases mentioned, will show other clinical signs of hypothyroidism.

Changes have been described in the small bones, especially in those of the tarsus, for example by Engeset *et al.* (1951) in three children with hypothyroidism. The age of the children at diagnosis was approximately 6, 10 and 12 months respectively. During treatment with thyroxine a strange *peripheral ring structure* was noticed, for example in the centres of the talus and calcaneus, with a peripheral, very dense zone, and internal to this a concentric clearing. These changes recalled to Engeset the picture in scurvy, but no lack of vitamin C was found. On examining the diaphysis of the long bones, corresponding cortical densities were found with clear zones lying within them. The changes disappeared after continued thyroxine treatment. One of the patients showed localised deformations of L. I-II, see below.

Similar changes were subsequently observed by others (Lelong *et al.* 1955), and the present author has observed them in many of his patients.

Multiple, accessory centres of ossification at the proximal ends of the metacarpal bones occur occasionally in hypothyroid children during treatment (Caffey 1957). Similar changes have been seen in the present author's patients (cases no. 21 and 31).

MULTIPLE DISTURBANCES OF OSSIFICATION (PERIPHERAL DYSOSTOSIS) IN THE PHALANGES OF THE TOES IN CHILDREN SUSPECTED OF HYPOTHYROIDISM

Looking for the above-mentioned accessory centres of ossification among other things, the author was struck by an observation which he had not seen previously mentioned. It was noticed that some of the children referred with suspected hypothyroidism, but who proved to be *euthyroid*, seemed to possess certain features in common. Their appearance recalls hypothyroidism—the condition first suspected. As a rule they are short and plump of build, the base of the nose is broad as in hypothyroid children, and most of them are mentally retarded. Otherwise there are no outward signs of hypothyroidism. Their colouring is normal. The skin is normal, warm and without mottling. I¹³¹ tests and the other tests for hypothyroidism are normal. Bone centres and dental development are retarded in some but not in others, and no hypothyroid dysgenesis is observed.

On the other hand, symmetrical changes in the phalanges of the feet have been a constant finding, resembling the changes described by Brailsford (1948)

under the name of "peripheral dysostosis", but which in his cases can occur both in hands and feet (see fig. 15), while the children described above show the changes only in the feet, especially in the four lateral toes. In a varying number of phalanges the proximal epiphysis is seen to be taper-shaped and wedged into the diaphysis, which is split like the end of an arrow.

Similar X-ray changes in the toes were described by Liess (1954), who considers that they occur quite frequently as non-specific changes, which perhaps can suggest developmental "reduction processes."

The present author has been unable to give any further explanation for their mode of origin, far less attach any specific significance to the changes, but as they seem to occur fairly often together with the other features described in children suspected of hypothyroidism, the occasion has been taken to mention them here. The author has never seen them in any of his hypothyroid patients.

Case reports

(I) Case record no. 1036/59, boy (fig. 9), 14 years old. Height 126 cms./normal 165 cms. Plump build, broad base of nose, mentally retarded, epileptic. Bone centre development corresponds to approximately 10 years. No hypothyroid dysgeneses. Dysostotic changes in the toes (fig. 16). At one time the patient was suspected of having hypothyroidism, but this diagnosis could not be maintained. I^{131} and other tests showed normal thyroid function.

(II) Case record no. 1475/56, girl (figs. 13, 14), 9 years old. Height 117 cm./normal 135 cms. Plump build, short extremities, lower segment 50 cm., upper segment 67 cm. Broad base of the nose. Has an apparently hypothyroid appearance. Mentally normal. Normal conditions shown in the various tests for hypothyroidism including I^{131} uptake. X-ray showed a slightly retarded bone centre development together with changes in the phalanges of the toes as shown in fig. 17. In addition a *Madelung's* deformity of the left radius was found. The parents and some of the siblings of the patient are small. Their skeletal structure has not yet been examined.

(III) Case record no. 431/58, girl (figs. 11, 12) $8\frac{1}{2}$ years old. Height 118 cm./normal 128 cm. Plump build. Wide inter-ocular distance. Resembles at first sight a "myxoedematous child". Mentally retarded. Constipated. The various thyroid function tests were normal, including I^{131} , X-rays showed a "retarded" bone development (about 6 years) without hypothyroid dysgenesis. The feet showed dysostotic changes as seen in fig. 17. Mother a little below average height. A younger sister reported to be of normal height. No X-ray examination of the family.

(IV) Case record no. 749/59, girl $10\frac{1}{2}$ years old. Height 135 cm./normal 142 cm. Appearance as in the patients described above. Treated with thyroxine for a number of years for suspected hypothyroidism. However, various tests

Euthyroid patients with a "hypothyroid" appearance and peripheral dysostosis of the first phalanges of the four lateral toes.



Fig. 9.
Case record no. 1036/59.

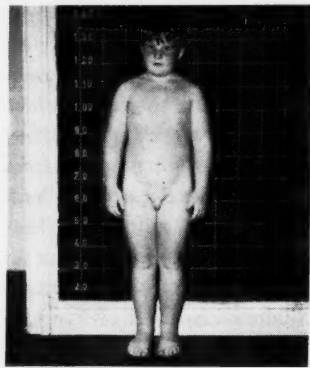


Fig. 10.
Case record no. 1091/58.

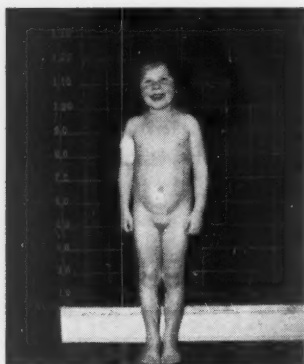


Fig. 11.
Case record no. 431/58.

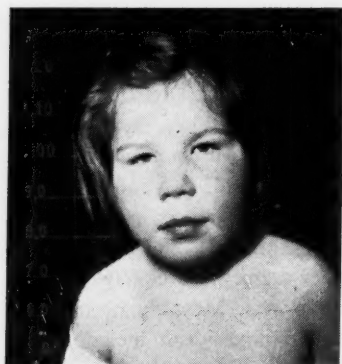


Fig. 12.
Case record no. 431/58.

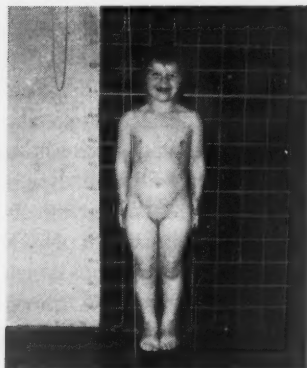


Fig. 13.
Case record no. 1475/59.

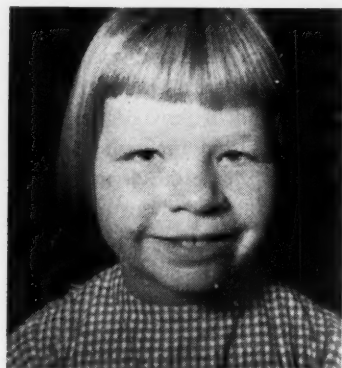


Fig. 14.
Case record no. 1475/59.



Fig. 15.

"Peripheral dysostosis".

Fig. 15.

Girl, 8 years old, with *Brailsford's syndrome*. The epiphyseal discs of the first phalanges are wedged into the shaft of the phalanges.

Fig. 16.

Boy, 10 years old,
case record no. 1091/58.

The picture shows a deformity in the four lateral toes similar to that of fig. 15.

Fig. 17.

Girl, 7 years old,
case record no. 27/51,
sister of patient in fig. 16, with same deformity.



Fig. 16.



Fig. 17.

showed euthyroid conditions both in this and a previous examination elsewhere. X-ray examination showed a normal bone age and no epiphysial dysgenesis, which in any case was not expected, as the patient had been given vigorous thyroxine treatment, as mentioned. Changes were found in the toes as shown in fig. 17.

(V) Case record no. 1091/58, boy (fig. 10), 10 years old. Admitted for observation for hypothyroidism. Height normal, 136/140 cm. Plump build with short broad feet, wide inter-ocular distance. Mentally normal. No sign of hypothyroidism on examination. X-ray showed normal bone development without any sign of hypothyroid dysgeneses. Changes in the toes as shown in fig. 16.

The sisters of this patient:

(VI) Case record no. 27/51 and fig. 17.

(VII) Case record no. 53/52 (Endocrine clinic), showed the same conditions in the toes. These children are both below average height like their brother and of normal intelligence. Both have been suspected of hypophyseal dwarfism but no endocrine abnormality could be demonstrated and their subsequent course has been euthyroid. The mother is of the same type. X-ray pictures of her are not available.

X-RAY CHANGES IN THE SPINAL COLUMN OF HYPOTHYROID CHILDREN

PREVIOUS STUDIES

In contrast to the very extensive literature on the peripheral epiphysial dysgeneses, only scanty reports are available on changes in the spinal column as a result of hypothyroidism in children.

The most frequently described radiological finding is a defect in the upper anterior part of the body of L. II, occasionally with similar defects in the adjacent bodies. *Evans* (1936) described a case like this, and in 1952 published a report together with an X-ray description of the spinal column in 12 other hypothyroid children, two of whom seem to have been atypical, as they reacted unsatisfactorily to thyroxine treatment. Seven of these thirteen children had the pronounced changes of the type described above, in the lower thoracic or the upper lumbar vertebral bodies, five had slight incipient changes, and one had a normal spine. *Evans* concludes that these changes in the spinal column are not congenital, that the kyphosis develops at the age of six months at the earliest, and that radiological changes then follow. Furthermore, he considers that improvement up to complete restitution can be obtained as a result of thyroxine treatment. In two cases, in whom the changes disappeared completely, the one patient had received orthopaedic treatment at the same time.

Bone changes without kyphosis were found in two cases, hitherto untreated when examined at the age of 4½ years.

The differential diagnosis from gargoylism and Morquio's syndrome is discussed; in these diseases, the spinal column also shows changes of somewhat similar appearance, and the suggestion is made that the localised lesions in the spinal column result from the basic systemic disease, causing a reduced resistance to mechanical stresses in the bodies of the vertebrae, these influences being greatest just at the transition between the lumbar spine and the thoracic spine; the result is that the changes take on a uniform appearance in these otherwise different diseases.

Swoboda in 1950 described seven cases of kyphosis with localised vertebral changes in the dorso-lumbar region in hypothyroid children. He points out that this may be a very frequent finding in this disease. Views which agree more or less with those above, are presented on the reduced resistance to mechanical influence, and in addition the parallel to Hurler's syndrome and chondrodystrophia foetalis is also mentioned. *Swoboda* does not include any examinations of children under six months of age, but considers that such changes must have a prenatal causation. Their mode of origin is also discussed especially with respect to whether the foetus depends on its own hormone production, or on that of the mother.

Thomsen & Vesterdal (1951), in an account of three cases of atypical Hurler's syndrome, drew attention to the similarity between the localised lesions in these cases and in hypothyroidism. The great retardation in the bone centres is stressed in the differential diagnosis, as this, together with the other clinical signs of hypothyroidism, distinguishes the two conditions.

General changes in the spinal column

Caffey's textbook (1945) draws attention to the retarded development of the spine in hypothyroid children, and shows two illustrations of three-year-old and 8-year-old children with flattened vertebral bodies, great inter-vertebral spaces, notching of the frontal surface of the body of the vertebra and remains of the foetal venous sinus together with open neurocentral synchondrosis.

Bamatter et al., in 1947, described a similar case, with instructive X-ray pictures, from a monstrously neglected case of hypothyroidism in a 13-year-old girl.

AUTHOR'S STUDIES

At the Nordic Paediatric Congress in 1954 (published in the Congress report), the present author submitted the results of a comparative study of the X-ray changes in the spinal column and peripheral skeleton in 14 children with treated or untreated hypothyroidism.

The results of this comparison showed that *the following general signs of retardation of the development of the spinal column: platyspondylia, broad intervertebral space, persistence of the anterior venous sinus, undeveloped articular processes, etc.*, were the characteristic findings in untreated or insufficiently treated patients (fig. 18). In general, the retardation of the spinal column ran a parallel course to the degree of retardation of the peripheral bone development (figs. 19–20), as was also to be expected. No changes were seen in the spinal column in the cases of late onset, nor were there any in those cases which had received adequate treatment for a prolonged period. The *localised* changes at the transition between thoracic and lumbar spine, which are described as particularly characteristic for this disease, *occur in only a minority of the cases*, which was in fact also to be expected if they are regarded as secondary phenomena. The youngest patient with local lesions of the spinal column of this type was 4½ months old, younger than any so far described.

Changes in the spine in older children with insufficiently treated hypothyroidism.

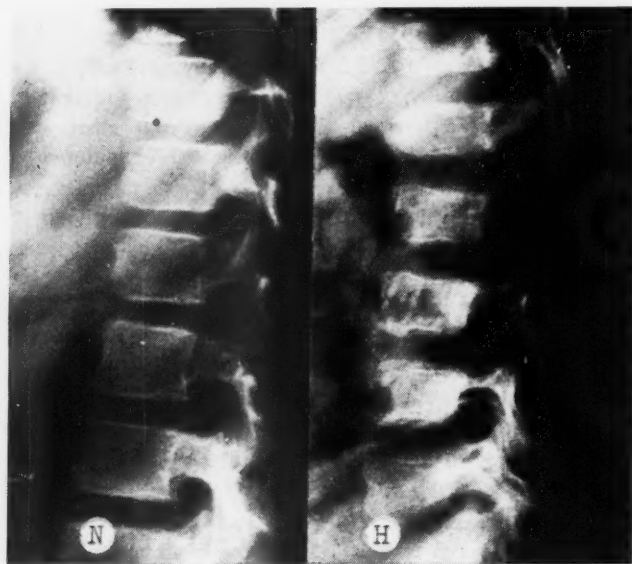


Fig. 18.

Normal child, 8 years old. — Hypothyroid child, case no. 21, 8 years old. Notice the wide I. V. disc spaces and the flattened vertebral bodies with persistent anterior notching of the upper lumbar and lower thoracic vertebrae. Retardation of the development of the vertebral processes is not clear in this picture.



Fig. 19.



Fig. 20.

Fig. 19. Epiphyseal dysgenesis (stippled epiphysis) of the hip of a 15-year-old boy with severe hypothyroidism.

Fig. 20 shows the spine of the same patient with similar but more pronounced changes than those described in fig. 18. The malformation of the vertebral processes is more obvious in this case. Notice the beaking of the body of the second lumbar vertebra.

The above mentioned general signs of retardation of the spinal column were not observed with any certainty in the youngest patients under the age of six months. On the whole, changes in the bone centres in the very young, apart from a few missing centres (see page 85), are poorly pronounced and quite atypical in hypothyroidism. The present author has been unable to judge whether or not the spinal column is retarded in development in very young hypothyroid children. In some cases, however, their appearance recalled the spinal column in premature children. On the other hand, changes were found within the bodies of the vertebrae strongly recalling those described by *Engeset et al.* (1951) in the case of the tarsus (see page 86). These changes were only slightly pronounced in untreated infants, but became very obvious after about 3-4 weeks' thyroid treatment, and disappeared after prolonged treatment (figs.

Changes in the spine ("double contouring") in insufficiently treated babies and young children with hypothyroidism.

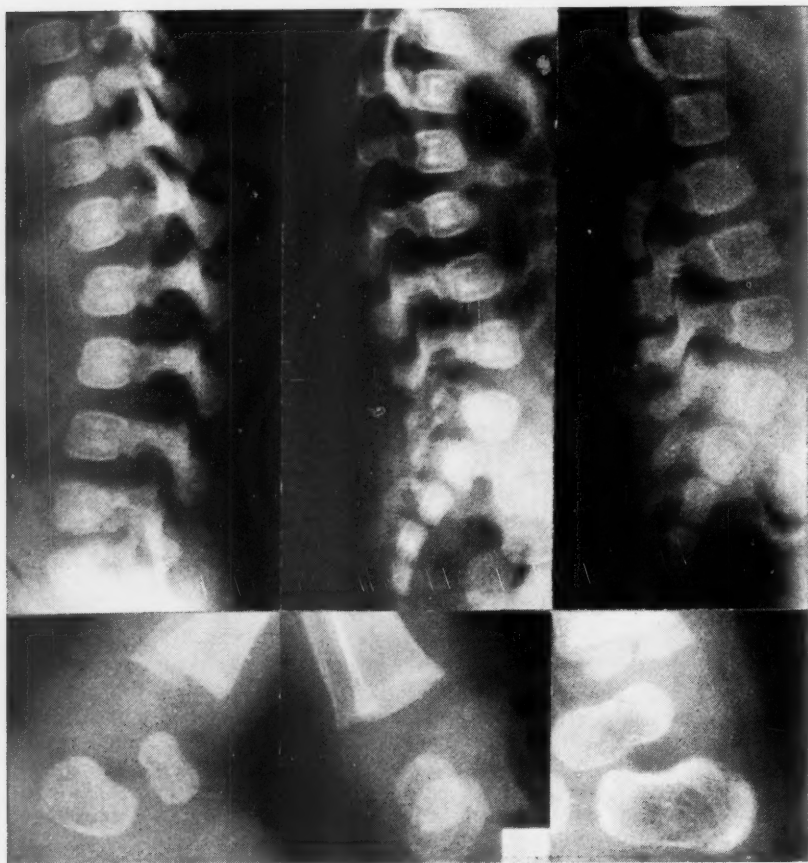


Fig. 21.

Shows corresponding changes in the spine and tarsus of: —

case no. 26 (left), 3½ months old, untreated.

case no. 2 (middle), 4½ months old, mild treatment.

case no. 2 (right) after 6 months' continuous treatment.

Notice the "double contouring" in the vertebral bodies and the foot, pronounced after a short period of treatment, and disappearing after further treatment.



Fig. 22. "Double contouring" of the vertebral bodies in case no. 14, $2\frac{1}{2}$ years old.

21, 22). The changes in the tarsus appeared and disappeared in complete synchronism with the processes described. The present author has not seen any previous mention of these changes, nor observed them in children with other diseases. Presumably, they must be regarded as "dysgeneses" of the spinal column. According to Caffey, ossification in the body of a vertebra normally proceeds from the surface of an ossification centre within the body, and increased activity here following treatment will appear as a condensed inner ring.

Table XIV shows corresponding studies on the patients discussed in the present investigation. A number of these were included in the previously mentioned material, and the last three patients in the table (indicated by case record numbers) belong to this, but as they have not been tested with I^{131} , they are not otherwise included in the material of the present study. Two patients (cases no. 25 and 38) are not included, as X-ray pictures of their spinal column are not available. With the exception of these two, the table thus includes all children with hypothyroidism examined since 1953, a total of 57.

The table shows that the observations reported at the beginning of this section appear to hold also for this extended material. It is seen in addition that patients no. 1 and 2, in whom the prenatal type of bone retardation is demonstrated, have no localised deformity. This tells against Swoboda's point of view, i. e. that such a deformity can be present prenatally, indicating therefore that the foetus was hypothyroid at that time. Cases no. 8 and 2, $3\frac{1}{2}$ and $4\frac{1}{2}$ months old respectively, show that changes can occur earlier than the age of 6 months, contrary to Evans' statement.

Table XIV.
X-ray changes in bone development in hypothyroidism.

Case no.	Age at spine X-ray	Previous treatment	Limbs		Spine		
			retard. development	epiphys. dysgen.	retard. development	"dysgenesis"	local changes
3	2 mth.	0	prenat.	—	!	"double contour" after treatment	—
6	2½ mth.	0	"	—		"	—
26	3½ mth.	0	" ?	+		"	—
8	3½ mth.	insuff.	"	+		"double contour"	L. III
2	4½ mth.	insuff.	" ?	+		"	L. II
33	1¾ yr.	0	R	+	R	"	L. II
14	2 yr.	insuff.	(R)	+	R	"	—
46	3 yr.	0	R	+	R	"	L. I-II
1	3 yr.	suff.	N	—	N	—	—
4	5½ yr.	suff.	N	—	N	—	—
5	14½ yr.	suff.	N	—	N	—	—
7	3 yr.	suff.	N	—	N	—	—
9	2½ yr.	suff.	R	+	R	—	L. III
10	13 yr.	suff.	N	—	N	—	—
11	11 yr	suff.	N	—	N	—	—
12	2 yr.	suff.	N	—	N	—	—
13	3 yr.	suff.	N	—	N	—	—
15	9 yr.	insuff.	N	—	N	—	—
16	8 yr.	suff.	N	—	N	—	—
17	8 yr.	insuff.	(R)	—	N	—	—
18	5 yr.	0	R	+	(R)	—	—
19	5½ yr.	0	R	+	(R)	—	—
20	12 yr.	insuff.	R	+	(R)	—	—
21	8 yr.	0	RR	++	R	—	—
22	8 yr.	0	RR	+	(R)	—	—
23	10½ yr.	insuff.	R	(+)	(R)	—	—
24	17 yr.	suff.	N	—	N	—	—
27	7 mth.	0	R	—	R	—	L. II
28	12 yr.	insuff.	R	(+)	N	—	—
29	13 yr.	suff.	N	—	N	—	—
30	1¾ yr.	insuff.	R	+	R	—	L. II
31	10 yr.	insuff.	R	+	(R)	—	—
32	13 yr.	insuff.	(R)	+	(R)	—	—
34	13 yr.	suff.	N	—	N	—	—
35	14 yr.	suff.	N	—	N	—	—
36	4½ yr.	0	R	+	R	—	L. II-III
37	6½ yr.	0	RR	+	R	—	—
39	13 yr.	insuff.	(R)	—	N	—	—
40	2½ yr.	suff.	N	—	N	—	—
41	1¾ yr.	0	R	+	(R)	—	L. III
42	9¾ yr.	suff.	N	—	N	—	—
43	10¾ yr.	suff.	N	—	N	—	—
44	2¾ yr.	0	RR	++	R	—	L. II

Table XIV contd.

X-ray changes in bone development in hypothyroidism.

Case no.	Age at spine X-ray	Previous treatment	Limbs		Spine		
			retard. development	epiphys. dysgen.	retard. development	"dysgenesis"	local changes
45	2 yr.	0	R	+	(R)	—	L. II
47	3½ yr.	insuff.	R	(+)	N	—	—
48	16 yr.	insuff.	R	—	N	—	—
49	7 yr.	suff.	N	—	N	—	—
50	7 yr.	0	RR	++	(R)	—	—
51	6 yr.	insuff.	R	+	N	—	—
52	10 yr.	0	(R)	(+)	N	—	—
53	12 yr.	0	RR	++	RR	—	—
54	12 yr.	0	R	(+)	N	—	—
55	14 yr.	0	R	(+)	N	—	—
56	16 yr.	0	R	—	N	—	—
1158/52	4 yr.	insuff.	RR	++	R	—	—
X-R. 1732/53	14½ yr.	insuff.	RR	++	RR	—	Th.XII-L.I
X-R. 1733/53	16½ yr.	insuff.	RR	++	RR	—	Th.XII-L.I

R = retarded. N = normal.

In the majority of cases the localized changes were small and disappeared quite rapidly during treatment. In some cases they were accompanied by kyphosis, in others not. The material is not extensive enough to allow an indication of actual lines of treatment of the localized deformities, but there is no doubt that the severe changes should also receive orthopaedic treatment. In the author's experience, the milder cases will become normalized after thyroid treatment alone. In one patient there was a severe deformity with kyphosis, where the kyphosis disappeared and the deformity became hardly visible. Treatment in this case was orthopaedic for the first 2-3 years.

Diagnostic value of the changes in the spinal column.

In infants with hypothyroidism, only few peripheral bone centres are found, so that changes in the body of the vertebrae can be of use in diagnosing hypothyroidism in such a case. The changes in the peripheral epiphyses in the later age groups seem to be more pronounced and better suited to diagnosing and dating the disease.

Familiarity with the general and the localized changes in the spinal column in hypothyroidism is also important in the differential diagnoses mentioned above—chondrodystrophy of various kinds, and also in cases where in the first instance only an X-ray of the spinal column is available and where hypothyroidism was not the clinical diagnosis.

CRANIAL CHANGES IN HYPOTHYROIDISM

Lusted et al. (1953), in their studies of the skeletal development of thyroidectomised young monkeys, found for one thing that the growth of the cranium as a whole was retarded, the closure of the sutures delayed, and the occipital bone thickened and flattened, appearing to grow more quickly and therefore over-running the parietal bone. In addition, the sella turcica was found enlarged, not only relatively but absolutely. The hypophysis was found correspondingly enlarged.

Similar changes have been described in man. *Engel et al.* (1941), in their studies of cranial and facial forms in hypothyroidism, state that the base of the cranium is shortened and that this is the result of under-development of the occipital and parietal bones in particular. In their study they review part of the older literature on the subject. *Caffey* (1957) finds that the retardation of the cranium is analogous to the retardation of the long bones, and he mentions the delayed closure of fontanelles and sutures. Further, differentiation of the cranial wall into laminae and diploë is delayed and incomplete, and pneumatization of the para-nasal bones and of the temporal bones is retarded. The same paper cites a study by *Dreyfus et al.*; these workers found a complete lack of cranial air sinus in 14 hypothyroid patients aged 6–35 years. According to these authors, this is a sign found only in congenital hypothyroidism. In the present material, the author has found that the para-nasal sinuses are strikingly small, in particular the frontal sinus, but has been unable to demonstrate a case where it has been actually absent. The changes disappear on treatment, and the present material contains only very few of the severe types of untreated congenital hypothyroidism in the age group in which a frontal sinus would be expected.

Caffey also cites a statement by *Silverman* who, in an unpublished study, repeatedly found the sella turcica enlarged in hypothyroid children, and associated this with an enlarged hypophysis. There are a number of previous communications on observations of this kind. Thus, in "The Thyroid" (1947) by *Means*, a number of pathological findings of enlarged hypophysis are cited in various forms of "cretinism", going right back to 1851. In addition, a series of single observations are available, both pathological and radiological, which confirm the above findings, *Olsen* (1935). *Hurxthal* (1948) also reports that in 35 cases of all types of "cretinism", the sella turcica was normal or enlarged.

In the present material, among the severe untreated or insufficiently treated cases, there are two patients with a strikingly large, ballooned sella surrounded by a dense osteosclerotic zone (see fig. 23).

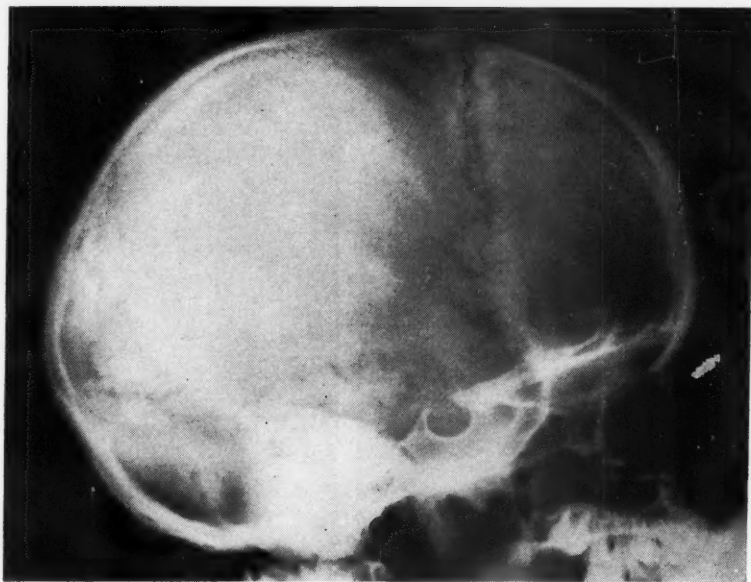


Fig. 23.

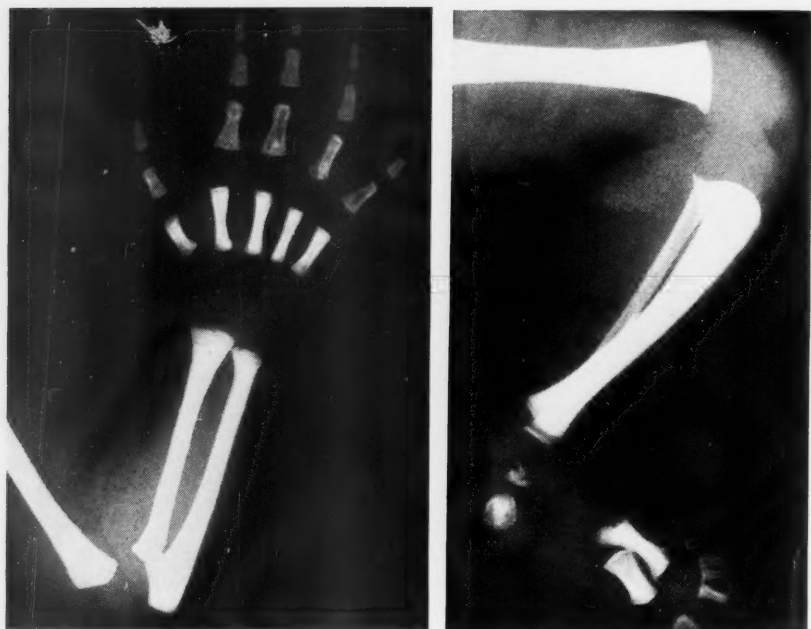
Changes in the skull in a 12-year-old girl, case no. 20, with insufficiently treated hypothyroidism. Notice the large, ballooned sella turcica, surrounded by an osteosclerotic zone.

CONGENITAL HYPOTHYROIDISM WITH OSTEOSCLEROSIS

In the above mentioned study by *Lusted et al.* (1953), on experimental athyrosis in young monkeys, the bony tissue was found to be sclerotic with a "density" 1.5 times normal.

A corresponding density is found generally in hypothyroid infants in parts of the base of the cranium and peripherally in the tarsus, vertebral bodies, proximal ends of the phalanges, etc. Occasionally, one encounters more *generalized osteosclerotic-like marble bones*. Figs. 24 and 25 show such a case (case no. 3). The changes disappeared in the course of about six months' treatment. It is striking that in this child, and in none of the other, early manifest cases, the enamel of the teeth has retained a remarkably "dense", dull, opaque structure.

As far as the author is aware, only a few similar cases have been described in the literature. *Jeune & Beraud* (1955) have published a case of osteopetrosis in a two-year-old child with severe, untreated hypothyroidism. Severe anaemia



Figs. 24 and 25.
Marbling in a two-month-old boy, case no. 3, with untreated hypothyroidism.

and hypoplastic bone marrow were also found. Nephritis developed during thyroxine treatment, which had to be temporarily withdrawn. The bone changes disappeared with continued treatment, but nephropathy developed. The nature of this was not determined, but the authors are inclined to assume that the basic cause for the changes in the bones was a kidney disease. They are supported in this by similar cases published by *Johnson & White* (1952) and *Royer & Megevand* (1954). In both cases quoted, a severe hypothyroidism was present, persisting for some time. In the first patient, the renal function was stated to be poor, and bilateral renal hypoplasia was demonstrated in the other patient.

There is nothing to suggest nephropathy in the present patient. He was examined repeatedly, and nothing in the subsequent clinical picture (with a period of observation of more than four years) supports this. Hypoparathyroidism seems excluded, both in the present case and in those cited. No examination for enamel hypoplasia was made in the above-mentioned studies. In the present case the dental changes, together with the early manifestation of the disease, suggest that the changes are of intrauterine origin. As mentioned, it

seems that primary or secondary renal disease, the result of hypercalcaemia caused by the release of calcium from the bones during treatment, can be excluded.

It is more likely that the changes are associated in one way or another with the experimental and also clinical observations of bone condensation in severe, untreated hypothyroidism, but why it is pronounced in this case, and not in the remaining cases of athyrosis of early onset, remains obscure.

Chapter IX

THE TEETH IN HYPOTHYROIDISM

THE DEVELOPMENT OF THE TEETH

The tooth "anlage" appears in the 6-7th foetal week at the 11-12 mm stage, as a down-growth (dental lamina) of the ectoderm of the oral mucous membrane. The enamel organ differentiates later. The formation of hard tissue begins in the 5th foetal month in the milk teeth with a deposit of dentine. Hereafter the inner enamel epithelium is converted to ameloblasts, and amelogenesis begins. The "anlage" of the permanent teeth develops from the original dental lamina, which grows in depth. In the case of the milk teeth, it is reckoned that enamel mineralisation begins in the 5-6th foetal month and is completed in the 4-12th month of life. It occurs in a definite sequence in the various teeth, and changes which interfere with the development and metabolism of the foetus, have the greatest effect on those processes of mineralisation which are in the course of development just at that time. The mineralisation process in the teeth is the most sensitive step in dental development, and changes here have no possibility of becoming normalized later. As mentioned, as the development and mineralisation of each tooth takes place according to a definite time scheme, extending over several years, and with very small individual variations, the changes later found in the enamel can be dated with fairly good certainty by means of time-tables for dental development.

Enamel hypoplasias, i. e. any disturbances of tooth formation revealed as macroscopically evident defects in the enamel, are seldom of *intra-uterine* origin except in hypothyroidism, even in severe maternal disease during pregnancy. On the other hand, birth itself gives rise to a demonstrable zone in the enamel. The number of *enamel hypoplasias of post-natal origin* increases strongly in the course of the first year of life, during which it reaches its maximum.

A Danish control material by *Lindeman* (1958) gives the frequency of enamel hypoplasias as 13 per cent. *P. O. Pedersen* (1944) found 15 per cent. These figures hold for enamel hypoplasias found in permanent teeth. No actual analysis is available for the frequency of enamel hypoplasias, including those of intrauterine origin, in the deciduous teeth. According to experience from

both this hospital (G. Holst, Dental Surgeon) and other sources, this frequency is much less than for the deciduous teeth.

The disturbances in mineralisation affect not only the enamel but also the dentine and the bony tissue surrounding the teeth, but the conditions for regeneration are better in these tissues than in the enamel.

DENTAL CHANGES IN CHILDREN WITH HYPOTHYROIDISM

It is a well-known clinical observation that dental development is delayed in hypothyroid children. It has been reported by many, e. g. *Wilkins* (1957), that bone age and dental age are both retarded to more or less the same degree.

However, a few studies have been made which suggest that dental development in untreated hypothyroid children is less retarded than bone development, and reacts more slowly to treatment with thyroxine (*Prader & Perabo* 1952, and others).

In most of these studies the dental development is evaluated on the basis of X-rays of the cranium, but not from special dental films suitable for evaluating the teeth. In hypothyroid children, examined clinically and with special dental films of the individual teeth, a number of whom are included in the present material, *Andersen & Holst* (1958) showed that the dental development is *less retarded* than the bone development in *untreated* hypothyroid children, that both become *normalized* after *adequate treatment*, and that *vigorous therapy* brings the bone development *ahead* of the dental development. It thus seems as if bone tissue reacts more strongly than dental tissue, both to thyroid hormone deficit and to thyroid hormone excess. Similar conditions hold with regard to the sex hormones (idiopathic precocious puberty) and adrenocortical hormones (adreno-genital syndrome) (*Prader & Perabo* 1952, *Andersen & Holst* 1958).

The factors operative in the delay of tooth eruption have not been clarified. A study by *Engel et al.* (1951) is remarkable in this connection. They found large amounts of mucopolysaccharides in the mucous gel surrounding the enamel organ, as a binding material between it and the surrounding connective tissue. During tooth eruption, at any rate, they were able to demonstrate in various experimental animals a depolymerization of this material, whereby the passage of the teeth was presumably eased. *Andersen et al.* (1955), in a study of mucopolysaccharides in the skin of children with hypothyroidism, showed that these substances are found in large amounts in the skin and subcutis of such children, and that they disappear on treatment with thyroxine. It is therefore reasonable to assume that a *corresponding process takes place around the teeth, and that an accumulation of muco-*

polysaccharides, as a result of a lack of depolymerization, contributes to tooth retention in hypothyroidism. As far as the present author is aware, no histochemical studies have been made of the connective tissue surrounding the teeth of hypothyroid children, but these conditions should be open to investigation by biopsy and histochemical analysis.

THE OCCURRENCE OF ENAMEL HYPOPLASIA IN HYPOTHYROID CHILDREN

Apart from a few general suggestions, for example by *Wilkins* (1957), that it is the structure of the teeth rather than their retardation which is characteristic of hypothyroidism, the present author has been unable to find any studies on the occurrence of enamel hypoplasia in hypothyroid children.

Thus, *Nordic Clinical Odontology* (1958) states "that hormonal influences on the quantitative course of the mineralisation other than parathyroid hormone do not appear to be demonstrated with certainty", and in *Cohen's Paediatric Dentistry* (1957) there is no mention of this.

In the study by *Andersen & Holst* (1958) quoted above, it was demonstrated that: *the number, form and size of the teeth were normal, but that the occurrence of enamel hypoplasia was unusually excessive* (80 per cent of the children examined), the figure normally being less than 15 per cent, (see above).

The intrauterine types of hypoplasia of the enamel appeared to be most common in the earliest manifest cases of hypothyroidism. These findings have been confirmed in the present larger and more differentiated material, and entered under the individual groups of hypothyroid children (pp. 46, 47, 54, 55, 70).

Bearing in mind the time for the appearance of the anlage as described above, the 6-7th foetal week, and the time for commencing mineralisation of the hard tissue, the 5th foetal month, in comparison with the time when the foetal thyroid gland commences its uptake of I^{131} , the 12-14th foetal week, and thus presumably commences its production of hormone (see page 109), it is reasonable to deduce that absent or reduced foetal hormone production will have no influence on the formation of the actual dental anlage, and thereby on the number of teeth etc., but will no doubt influence the mineralisation of the enamel. This agrees with the clinical findings. Even though enamel hypoplasias, as mentioned, are non-specific for absence of thyroid hormone, they nevertheless do appear to possess significance in attempts to date the origin of hypothyroidism, and in elucidating whether the athyrotic foetus is sufficiently covered with maternal hormone in pregnancy and the early post-natal period.

CARIES FREQUENCY IN HYPOTHYROID CHILDREN

Light was cast by the investigation mentioned on a further point, namely the question of *caries frequency in hypothyroid children*. This is generally stated to be great, but in our material the order of magnitude was found to be *the average for children* at the age in question.

In many of the hypothyroid children, and most pronounced in the untreated ones, signs were found of retarded mandibular development, infantile mandibular angle, traces of the effect of macroglossia, etc., as well as absent root resorption. The structure of the jaws and facial skeleton in hypothyroid children has previously been studied by *Engel et al.* (1941).

Chapter X

THE FUNCTION OF THE THYROID GLAND IN THE FOETUS

PREVIOUS STUDIES

As will be understood from the previous discussion, see for example pp. 45, 49, there is no agreement on whether the thyroid gland in the foetus has an independent function—and if so whether this function is an adequate one.

This discussion is of older date, and its earlier stages will not be reported here. They will be found discussed by *Dorff*, who in 1934 was the first to demonstrate signs of intrauterine bone retardation in a twin with congenital hypothyroidism and a normal twin partner, in whom bone development was normal. *Dorff* deduced from this, for one thing, that the foetus has an independent thyroid activity which while not particularly great, is adequate, and not directly affected by the thyroid hormone of the mother. Further, he showed that there was presumably no transmission of thyroid hormone via the placenta, either from the mother or from the foetus. *In Dorff's opinion*, there is no use for thyroid hormone in the earlier stages of foetal life, and the foetus's own thyroid gland, as stated, is normally able to meet the rather modest demands made on it *in utero*. When the thyroid gland of the foetus is defective, this is the result of a disturbance of development, and hardly the result of infection. The defect will be manifest *in utero* by bone retardation, and the requirements of the foetus will not be covered by the mother's thyroid hormone. Nor are the post-natal requirements of the infant met by a depot of thyroid hormone handed on by the mother, or by hormone transferred with her milk.

Subsequently, other workers found a corresponding condition of "pre-natal" bone development in athyrotic infants, see for example *Wilkins* (1957), and they agree with *Dorff* in his interpretation of these findings as a sign of intrauterine hypothyroidism. The present author's studies discussed on pages 45–48, 54, 55 are in accordance with this.

Others, again, still share the opinion of *Kocher* (1892), namely that the thyroid hormone production by the mother covered the requirements of the foetus and of the newborn infant. Thus, *Reilly* (1957) and *Pickering & Fisher* (1958) maintain that a euthyroid mother with a normally functioning placenta

will usually be able to supply an athyrotic foetus with thyroid hormone in an adequate manner, and also cover the requirements of the newborn infant during the first few weeks.

Whatever significance one attaches to the bone findings mentioned, particularly the absence of the lower femur centres in infant athyrotics—and the present author believes that it is a frequent finding, provided it is searched for in a consistent manner—they can only be an indirect measure of thyroid function *in utero*. Numerous studies have been made of thyroid function and placental permeability for thyroxine in animal foetuses. However, as circumstances differ widely from one species to another, and can hardly be directly compared with conditions in man, such studies will not be discussed further.

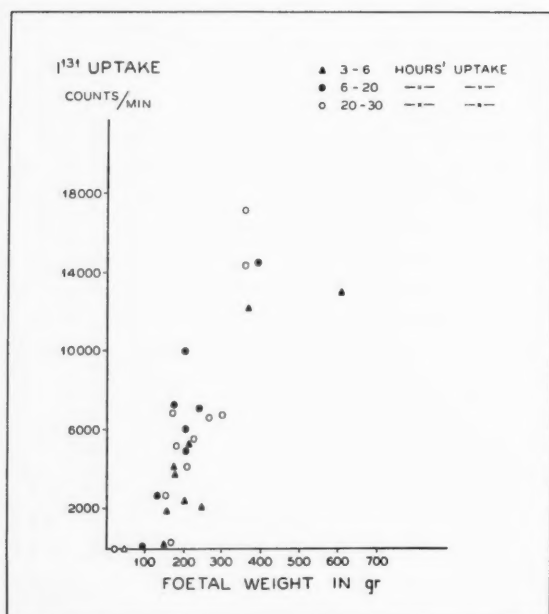
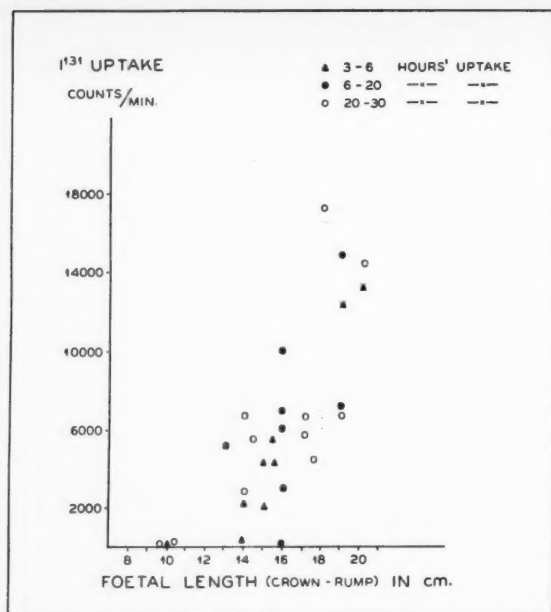
As to the thyroid in the human foetus, we know for example that its cells appear around the third foetal week, and that follicles and colloid form around the 13–14th foetal week. *Elmer & Scheps* (1935) demonstrated thyroxine in the foetal thyroid at this point of time (third month). *Chapman et al.* (1948) demonstrated that after the intake of I^{131} in mothers prior to abortus provocatus, the thyroid gland of the foetus accumulated iodine and presumably produced hormone from the 12–14th week. *Hodges et al.* (1955) found corresponding results. *Grumbach & Werner* (1956) showed that labelled thyroxine passed only very slowly through the placenta into the foetus. *McClendon & McLennan* (1939) found that the concentration of hormone-bound iodine was often much less in the foetus than in the mother, while most other workers, for example *Pickering* (1958), maintained that there is no difference.

Finally, *Robbins & Nelson* (1958), studying fractionated and protein-bound thyroxine in the newborn and in pregnant women, found a higher concentration of *free thyroxine* in the foetus than in the mother; in their opinion the result of the foetal thyroid action.

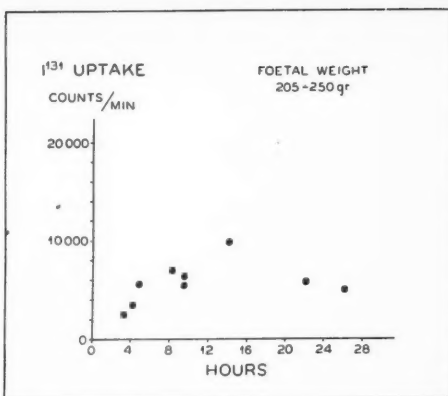
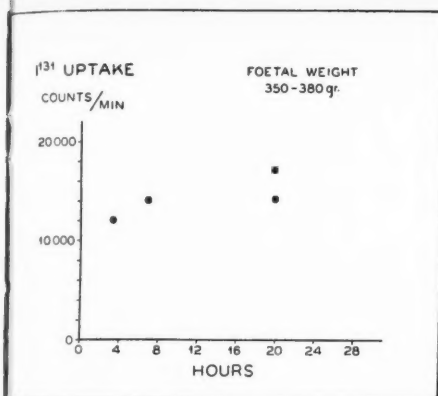
It will be seen from the discussion that the circumstances are complicated and far from clarified. It is possible that the factors at work are not alternatives, but factors in combination, and that individual differences probably play a part. The possibility cannot be excluded that thyroxine from the mother, by diffusion through the placenta, covers *a part* but *not all* of the thyroid requirements of the foetus, and that the deficit thus acts as a stimulus for the production by the foetal gland, which normally covers the remainder of the requirements.

AUTHOR'S STUDIES OF FOETAL UPTAKE OF I^{131}

At the Nordic Paediatric Congress in 1958, the present author submitted the results of a study of I^{131} uptake in the thyroid gland of the foetus. The studies were carried out in collaboration with *J. Lind*, Stockholm, and *H. Levi*, Copen-



Figs. 26 and 27. Uptake of iodine¹³¹ in the foetal thyroid, compared with foetal length and weight respectively (see p. 109).



Figs. 28 and 29.

A comparison of iodine¹³¹ uptake by the foetal thyroid (ordinate) and the interval between maternal intake of iodine¹³¹ and operation (abscissa), in two groups of foetuses of approximately the same weight in each group (205-250 gm. and 350-380 gm. respectively). (see p. 110).

hagen, on a Swedish abortion material, the autoradiography of the foetuses being carried out by H. Levi. The procedure was that approximately 30 μ C of I¹³¹ was given to the mothers at varying intervals before the abortion was carried out. After the operation, various foetal organs were examined, including the trachea and the thyroid gland. The thyroid gland was dissected out and a measurement of the radioactivity in the remainder of the tracheal preparation was made to ensure that all the thyroid tissue had been included. After the measurements, autoradiographs were made of the tissue of the thyroid gland. These studies agree in general with the results of measurements of the total activity of the gland in the scintillation counter, and will be published later.

It will be seen from table XV and figs. 26 and 27, that after about the 10-12th foetal week, determined according to the weight of the foetus and the crown/rump length in centimetres, iodine began to accumulate in the thyroid gland, and that the activity increases more or less uniformly and strongly according to weight and length throughout the whole period of study and until about the 25th week.

A corresponding relationship, not represented here diagrammatically, was found to exist between the weight of the thyroid gland and its activity. By measuring the amount of radioactivity ingested and the amount demonstrated in the thyroid gland, the uptake in the thyroid gland was calculated as being between 0-2 per cent of the radioactive iodine ingested.

Various signatures are used in the figures according to the time elapsing

Table XV.
Iodine¹³¹ uptake in the foetal thyroid.

Case record no.	Sex	Foetal weight, g	Thyroid weight, mg	Crown-rump length, cm	Interval maternal intake I ¹³¹ -operation	Counts per minute
1947/56 SBB.....	F	225		15½	5½ hrs.	5,475
1449/56 SBB.....	M	189		15½	5 hrs.	4,005
1987/56 SBB.....	F	373		19	3½ hrs.	12,214
2142/56 SBB.....	M	252	210	14	3 hrs.	2,190
2187/56 SBB.....	M	200	122	16	4 hrs.	2,694
2186/56 SBB.....	M	185	190	15	4½ hrs.	4,174
402/57 SBB.....	M	610	406	20	4 hrs.	13,000
524/57 SBB.....	F	40	78	10	4 hrs.	100
563/57 SBB.....	F	160	193	14	4 hrs.	350
699/57 SBB.....	F	155	144	15	6 hrs.	2,000
928/56 SBB.....	M	200	110	16	15 hrs.	10,035
2254/56 SBB.....	A F	205	219	16	9 hrs.	6,030
	B F	212	173	13	9 hrs.	5,166
2252/56 SBB.....	M	177	135	16	10 hrs.	7,110
615/57 SBB.....	F	380	206	19	7 hrs.	14,900
714/57 SBB.....	M	240	161	19	8 hrs.	7,000
759/57 SBB.....	M	145	114	16	7½ hrs.	2,800
763/57 SBB.....	M	110	118	16	10 hrs.	100
3981 SBB.....	M	265	189	17	56 hrs.	6,704
3973 SBB.....	M	185	96	14½	24 hrs.	5,487
3979 SBB.....	M	210	150	17½	25 hrs.	4,382
4212 SBB.....	M	140	77	14	23 hrs.	2,961
4192 SBB.....	M	360	220	20	20 hrs.	14,481
4210 SBB.....	M	220	209	17	23 hrs.	5,703
973/57 SBB.....	M	30	31.6	10	24 hrs.	0
1203/57 SBB.....	M	350	146	18	20 hrs.	17,200
1222/57 SBB.....	M	145		14	20 hrs.	6,700
1315/57 SBB.....	M	305		19	21 hrs.	6,800
1364/57 SBB.....	M	160		10	22 hrs.	300

SBB = Södra Barnbördshuset, Stockholm.

between intake of I¹³¹ and when the abortion is performed, i.e. the time available for the iodine to accumulate in the thyroid gland. Within rather wide limits, this time does not appear to influence the final result. This must presumably signify that an equilibrium is established rather rapidly in the thyroid gland between uptake and output. This is confirmed by plotting the activity in foetuses of approximately the same weight, but where the time intervals between the intake of I¹³¹ and interruption of pregnancy were of varying lengths. As the dose was the same in all cases, a rough uptake curve can be drawn from these measurements (figs. 28 and 29), showing that the uptake reaches a level after about six hours. This level is reached earlier than the corresponding one in children and adults (see fig. 1 p. 34), and the

greater activity found by some workers during the days just after birth (page 22) could fit in with this.

In some of the foetuses, particularly at the start, all the organs were examined for radioactivity by means of the scintillation counter. In no case could radioactivity be demonstrated outside the thyroid gland. Studies of the kind described above thus suggest that the thyroid gland in foetal life has an independent function (the accumulation of iodine being a necessary, but not a sufficient condition, for the functioning of the thyroid gland). However, they are also of significance for determining the time at which damage to the thyroid gland of the foetus might be expected with intake of I^{131} , for example in the treatment of thyrotoxicoses in the mothers, as mentioned by *Chapman* and by *Hodges et al.*

FINAL REMARKS

In this study, the author's efforts were directed towards as early and as specific a diagnosis of primary (thyrogenic) hypothyroidism as possible. The results obtained are indicated in the individual sections, and in what follows an attempt will be made to review the position today, and examine the possible direction of future work.

In children with hypothyroidism, particularly the athyrotic form that becomes manifest early in the first year of life, and also in the severe forms of hypoplasia and enzyme defects, the most important question is: how can the mental prognosis be improved? As far as the author can judge from his own experience and that of others, the permanent intelligence defects in these children are in most cases the result of the influence of a hypothyroid condition on the brain development in utero and soon after birth. The best results have been achieved by vigorous treatment started within the first three months of life, (see pages 40-43), but even in these cases the results are far from good, and apparently capricious. In addition, the majority of the cases with early symptoms, reported both from Denmark and abroad, come to treatment at a later stage, giving correspondingly poor results. The efforts to obtain better results must therefore continue to be based on recognising the disease at as early a stage as possible.

One of the ways of achieving this is improved knowledge of the various forms of the disease and their heredity. In genetic analysis, it is *important that the nature of the defect in each individual clinical picture be elucidated as far as possible*. In addition, the *family should be examined* with respect to manifest and latent thyroid disease. Such a genetic analysis of the information thus collected should make it possible in future to reach an improved evaluation of the risk of hypothyroidism developing in the individual pregnancy. Studies of this kind have been made: *Bernheim et al.* (1954), *Mosbech et al.* (1957) and others. However, the series are generally rather small and the differentiation not particularly thorough. Further, the results are contradictory.

Information such as this must constitute the basis of the work, if there is to be hope of attacking a hypothyroidism in utero by treatment of the mother in pregnancy, a method which would seem to be of value both theoretically and practically. In such a case it would also be necessary to know which hormones or hormone fractions could reach the foetus without damaging the

mother or resulting in undesirable side-effects in the foetus. As far as the author is aware, such experiments have not been made in man, and animal experiments as mentioned on page 107 hardly permit direct conclusions. However, it would seem possible to trace some of these relationships, for example by making use of legal abortions.

A knowledge of the heredity could arouse suspicion of hypothyroidism in the newborn infant. In a corresponding manner, consanguinity in the parents (especially cousin marriage), reports of postmaturity, over-weight children, severe, persistent icterus neonatorum, etc., should contribute to a heightened watchfulness for signs of congenital hypothyroidism. In a newborn child the presence of a congenital goitre, large or small, especially in those cases where the influence of goitrogenic substances is unlikely, is even more significant than the above-mentioned non-specific signs and circumstances.

All children with congenital goitre, or whose condition in any other way is suggestive of congenital hypothyroidism, should be examined for this as rapidly as possible. The demonstration of absent lower femur centres is important in this connection (see pages 48, 85), for which reason X-ray examination of the knee joint or possibly of "half a skeleton", should replace X-ray films of the hand, the development of which shows a much greater range of variation. The author is also inclined to believe that *X-ray examination of the dental development*, even in very young babies, would be found of value in determining a retarded prenatal development. The determinations of the protein-bound iodine and possibly butanol-extractable iodine are very useful aids to diagnosis when evaluated together with the other findings. At this age, serum cholesterol determination can hardly be ascribed any great value. In cases of doubt, or to elucidate special conditions, the intake of radioactive iodine might be considered, either small amounts (0.25 μC) of I^{131} , or I^{132} , which breaks down much more rapidly, and is well suited to studies of brief duration. If possible, the iodine tests should be performed in association with chromatography of the urine. If the above tests prove negative, but the development of the child during the subsequent period still suggests hypothyroidism, the tests should be repeated.

In the immediate post-natal period, the signs which should be looked for in a child in whom hypothyroidism is suspected are not merely the classic ones familiar from the illustrations in many textbooks. Such signs—macroglossia, cool, mottled, myxoedematous skin, often first presenting as flabby wrinkles in the forehead, coarse hair, etc., usually do not appear until some months have elapsed. The first clinical signs of bodily and mental retardation, characteristic of the decline of thyroid function, are usually a *stagnation of growth in height* together with a more or less striking "placidity" and torpor in the child, often in connection with increasing *loss of appetite* and constipation, which can rapidly reach a severe degree. In certain cases these children have

been thought to be suffering from megacolon. Individually or in combination, these signs are nonspecific, but they should nevertheless also awake suspicion of hypothyroidism. The child should be seen frequently, and if they persist or if the more classic signs begin to appear, the child should be examined by some or all of the tests previously mentioned. Umbilical hernia often occurs, but is so common in the newborn that by itself it has no significance. On the other hand the voice quite rapidly develops a remarkable, characteristic, gruff and husky tone. Snoring and noisy respiration, especially when the macroglossia becomes pronounced, is not uncommon. Cases of collapse with cyanosis, possibly simulating heart disease, at times with fatal outcome, are reported to be common, but the present author can recall only two cases, the one in connection with the aspiration of food, the other of unknown cause.

When the fully-pronounced picture of congenital athyrosis or severe hypothyroidism has developed, often in the fifth to sixth month, the diagnosis presents no difficulty, but by then, as mentioned, the prognosis is already considerably less favourable.

The more insidious forms of hypothyroidism, depending on the retention of a portion of thyroid tissue but not enough to meet the requirements of the body in the long run, can be difficult to recognise, but if a look-out is kept for the more general deficiency symptoms, as well as for the classic signs of the disease, there will be a possibility of early diagnosis. In the case of the forms of late manifestation (8-14 years), the stagnation of growth in height is once more of value in diagnosis, and found for example from the measurements made by the school medical officers.

Further features are constipation, sluggishness and a certain lack of mental initiative (there is difficulty with arithmetic in school). It was striking how often the present author found the symptom of "tiredness" as a main complaint in these children. The degree of mental reduction or lack of development varies very much. For example patient no. 22, untreated, had an I. Q. of 121 and was the best in the class. Stagnation of growth and inhibition of bone centre development, possibly with dysgenesis, are constant phenomena. On the other hand these children are very rarely over-weight to any great degree, contrary to the still very common belief.

Measurement of the oxygen uptake, "the basal metabolism", is not very much used at present in the diagnosis of hypothyroid children. The apparatus usually employed is not convenient for infants and small children, and special equipment is available in only a few clinics. In addition the method is very unspecific. Calculated per unit of surface, most older hypothyroid children will have too low values of oxygen uptake, but a number of adipose and also thin euthyroid children will fall outside the normal range. It is still not altogether unusual for adipose children, otherwise of healthy appearance and vigorous growth, to be put on thyroid treatment because of a "metabolic test"

of about 80–85 %. The determination of protein-bound iodine (P. B. I.) or better still B. E. I. (butanol-extractable iodine), considered to represent the hormone-bound iodine, is of great value in most cases, and perhaps the best single criterion of thyroid function available at the moment. As mentioned, the results should be evaluated against a background of the patient's other symptoms. Certain forms of hypothyroidism, particularly accompanied by goitre, may show high serum values of hormone iodine, possibly representing hormone fractions which are biologically less active. Iodine-containing medications, the use of urography, etc., prior to P. B. I. measurement may give elevated values. However, the methods still require rather large amounts of blood, which is a disadvantage, especially in repeated examinations of infants. As mentioned on page 107 it is presumably the amount of free thyroxine in the blood that plays a particular role for the thyroid status of the patients, and micromethods for a reliable determination of this would be most desirable in paediatrics.

The possible future significance of radioactive iodine studies cannot be stated with certainty. The weightiest objection to these studies is the introduction of radioactive substances into the children. With the continually improved techniques available, however, the doses have been brought down, as mentioned, to a very low level. In each individual case, the risk must be very carefully weighed up against the gains. Hereby one must at all times remember that a condition of hypothyroidism which is overlooked is a very serious matter in a child, and that we still have no diagnostic procedure which is completely sure in all cases. In the differentiation and study of certain forms of hypothyroidism, and in the diagnosis of doubtful cases, I^{131} studies have made a considerable contribution where the other aids have failed. Until further, therefore, it seems reasonable to continue to use this method of investigation in special studies—possibly replacing it by the use of I^{132} in the cases where this is possible.

Diagnosis and treatment *ex juvantibus* has been and is still a much employed method. However, out of consideration for the patient—who otherwise must continue a possibly unjustified treatment all his life—as well as with a view to a general clarification of the disease as a whole, an attempt should be made at some stage or another to verify the diagnosis by other methods such as mentioned above. If, as a result of an erroneous surmise of hypothyroidism, a euthyroid patient has received thyroxine for some time, his thyroid function will be inhibited and may possibly have ceased completely. During the period after withdrawal of the treatment, and before the patient's own thyroid gland has achieved full function, presumably after 4–6 weeks (whether it can do this in all cases is not known) the patient will develop symptoms of hypothyroidism. If this is not realised, it is possible to draw the erroneous conclusion that these symptoms prove the accuracy of the diagnosis.

In conclusion, it must be said that though recent years have seen greater clarification of the nature of hypothyroidism, there is still much remaining unexplained. However, there is so much fresh knowledge, inspiring for future study, that the justification for the rather pathetic aphorism of Lisser in 1951 will also be recognised even in the future:

"Learn ye well all the conspicuous peculiarities but also the capricious vagaries and hidden hints of thyroid failings, and much misery will be spared your patients and much satisfaction added unto you."

SUMMARY

In the *introduction*, *hypothyroidism* in children is defined as any hypofunction of the thyroid gland which affects the growth and development of the child. The designation is used to describe the clinical picture throughout the whole course of childhood, instead of such names as congenital and acquired myxoedema, cretinism, etc. *Athyrosis* is the most severe degree of hypothyroidism.

The work consisted in the main of examining a series of hypothyroid children by means of tests with radioactive iodine, supplemented by other studies, in the first instance examinations of the bones and teeth. The aim was, first to arrive at as early and sure a diagnosis as possible, and secondly to try and sort the hypothyroid children into as uniform groups as possible, according to type and degree of thyroid defect, with the intention of arriving at an improved evaluation of the progress, the effect of treatment, etc.

Chapter I gives the history of hypothyroidism and the various views on its etiology. The literature on the mental prognosis for these children is also reviewed here, this being the most important and most discussed clinical problem.

Chapter II reviews studies of the uptake of radioactive iodine (I^{131}) in euthyroid children. The author's own procedure is described. In 44 euthyroid patients aged 8 months to 17 years, whose symptoms had suggested hypothyroidism, the mean percentage uptake of I^{131} was found to be 43.5 ± 1.5 after 24 hours, with a standard deviation of 9.7.

Chapter III discusses previous studies, including those by the author, on the uptake of I^{131} in hypothyroid patients. The author's material comprises all those children with primary (thyrogenic) hypothyroidism, examined by means of the above-mentioned technique at Queen Louise's Children's Hospital during the last five years. Cases of secondary (hypopituitary) hypothyroidism are not included in the present material. Three groups could be distinguished :

Group I: 24 children with very reduced or no uptake of I^{131} over the thyroid gland.

Group II: 14 children with exclusively ectopic, sublingual I^{131} uptake.

Group III: 18 children with hypothyroidism and goitre.

This distribution deviates considerably from what is found in other series. The reasons for this are discussed under the separate groups.

Group I comprises patients with athyrosis and hypoplasia of the thyroid gland. In these patients, the uptake of I^{131} lies far below that of euthyroid subjects. Quite good correlation is found between the amount of radioactivity measured over the thyroid gland, the age at onset of symptoms and the age at diagnosis.

As far as the mental prognosis is concerned, the results suggest that if athyroid children (uptake = 0) receive vigorous and regular treatment prior to the fourth month of life, it would seem that at least some of them may achieve the level of normal intelligence. If the treatment is instituted after the fourth month, the chances of normal intelligence will be very small. Children with an I^{131} activity over the thyroid gland of 10 % or more are not usually diagnosed until after the first few years of life, and most often their intelligence will be normal.

Among other features of the patients in *Group I*, it might be mentioned that no association has been demonstrated between the age of the mother and lack of thyroid in the child. With few exceptions, the mothers have not suffered from disease of the thyroid during pregnancy. Pregnancy and labour have generally been normal, although showing a tendency to "postmaturity". In two patients, a positive toxoplasmosis reaction was found in mother and child. The significance of this is not clarified.

The serum cholesterol value was generally elevated in all three groups, while the protein-bound iodine in the serum was reduced, with some few exceptions.

A comparison of birth length, bone development and dental development in athyrotic infants in this material reveals the interesting fact that bone and dental development are prenatally retarded, suggesting intrauterine hypothyroidism, while the birth length is normal or even above normal. The literature gives no exact figures for the birth length in athyrotic children. The factors are discussed which might contribute to the growth of the athyrotic foetus. Attention is drawn to the function of the foetal adrenal cortex.

Chapter IV reviews the foetal development of the thyroid gland, particularly its descent from the root of the tongue to its final site in the front of the neck.

Group II: 14 patients are then described in whom non-palpable, sublingual, ectopic thyroid tissue was the sole site of uptake of I^{131} . The author demonstrated this foetal malformation in an infant with "congenital" hypothyroidism of rather slow progression. It was demonstrated elsewhere that a condition such as this could be the cause of some cases of "acquired" hypothyroidism.

As a result of systematic examination of all children without I^{131} uptake over the normal site of the thyroid gland, the malformation described was found in 14 of a series of 56 hypothyroid patients examined, and may therefore be regarded as not nearly so uncommon as previously assumed. Children

of this type present their symptoms somewhat later than the athyrotics, and the prognosis is correspondingly better. In other respects, the group can be associated with the Group I hypoplasias of the thyroid gland.

The sex distribution for Groups I and II together is that usually given in the literature: twice as many girls as boys. However, if the cases diagnosed before the age of 6 months are considered, the distribution is found to be equal between the sexes, while for the cases diagnosed after the age of 6 months, the proportion is still about twice as many girls as boys. Grouping a number of similar series together, the same difference is apparent, and appears to be significant at the 5 per cent level.

Chapter V commences with a description of the normal hormone production of the thyroid gland, and the disturbances in the production, either as a result of lack of iodine (*endemic cretinism*), or disturbances of hormone synthesis on account of congenital enzyme defect and the like.

Group III: The author describes 18 patients with hypothyroidism and goitre, and attention is drawn for one thing to the pronounced familial disposition and to the occurrence of a large number of deaf-mute children (about $\frac{1}{3}$) in this group. The reason for this is discussed. At the time of diagnosis the children in Group III are on the average older than the children in Group I. The age distribution is illustrated for all three groups.

The various uptake curves for I^{131} are discussed, and the histological findings described in some thyroidectomized patients in this group.

Chapter VI, on the basis of a review of the literature, discusses hypothyroidism as a sequela of extrathyroidal enzyme defect, and hypothyroidism as a sequela of auto-immunization (Hashimoto's struma).

Chapter VII discusses the relationship between "simple" goitre and hypothyroidism with goitre. The author's studies of 28 euthyroid children with goitre are discussed, with an account of familial incidence, uptake of I^{131} , content of protein-bound iodine in serum, etc.

Chapter VIII discusses the X-ray changes in hypothyroid children. The typical epiphyseal changes in the long bones, the dysgeneses, are mentioned, together with the diagnostic significance of these findings. Further, cases are described of a type of euthyroid child of hypothyroid habitus, with "peripheral dysostosis" of the toes, a condition apparently not previously mentioned in the literature. These children had all been erroneously regarded as hypothyroid.

The X-ray changes in the spine are described, both the localised deformities at the transition between the lumbar and thoracic spine and—more characteristic—the general retardation of the spine. These changes progress more or less parallel with the retardation in the peripheral bone development. A spinal

type of "dysgenesis" of the vertebral body was described by the author in 1954. These findings are discussed.

The roentgenological picture of the cranium in hypothyroidism is described, with particular reference to the size of the sella turcica, and the significance of this discussed.

An unusual case is presented of apparent, temporary osteopetrosis in an athyrotic infant, who at the same time showed persisting changes in the enamel of the teeth.

Chapter IX reviews the author's studies of the teeth in hypothyroid children. It is stressed that the size, number and shape of the teeth are normal, whereas the enamel is hypoplastic and dysgenetic. This fits in with the times for the appearance of the tooth "anlage", enamel formation and foetal thyroid gland function. *Studies of the frequency of enamel hypoplasias (present in about 80 per cent of the hypothyroid children examined) may be used, for example, to estimate whether hypothyroidism has been present prenatally, as such changes (acquired in utero) are very rarely observed in normal children, or in children with other diseases, and the changes do not disappear during thyroid treatment.*

Dental development is, in general, less sensitive to changes in the thyroid status of the organism than bone development. The same is also the case for other hormones, for example sex hormones and adrenocortical hormones.

Chapter X describes previous studies of foetal I^{131} uptake in man. The conclusion of the author's studies is that the foetus takes up I^{131} in the thyroid gland—but not in demonstrable amounts at other sites—from about the 12th–14th week of pregnancy, and that the gland appears to be very active.

The *final remarks* discuss in particular the question of early diagnosis, together with the possibilities of genetic prophylaxis and intrauterine treatment of the foetus by treating the mother.

RESUMÉ

I *indledningen* defineres *hypothyreose* hos børn som enhver underfunktion af gl. thyreoidea, der påvirker barnets vækst og udvikling. Betegnelsen anvendes om sygdomsbilledet gennem hele barnealderen i stedet for navne som congenit og aquisit myxoedem, kretinisme etc. *Athyreose* er den sværeste grad af hypothyreose.

Arbejdet har væsentligt drejet sig om at undersøge en række hypothyreoide børn ved hjælp af radioaktivt jod suppleret med andre undersøgelser, i første række knogle- og tandundersøgelser. Formålet har været at finde frem til en tidlige og sikrere diagnose. Endvidere har man villet prøve at differentiere hypothyreoide børn ud i så ensartede grupper som muligt efter arten og graden af deres thyreoideadefekt af hensyn til vurdering af prognose, effekt af behandling etc.

I *kapitel I* omtales hypothyreosens historie og forskellige opfattelser vedrørende ætiologien. På dette sted gennemgås endvidere litteraturen om den mentale prognose, der er det vigtigste og mest omdiskuterede kliniske problem.

Kapitel II indeholder en oversigt over 131 tidligere undersøgelser af optagelse af radioaktivt jod (J^{131}) hos euthyreoide børn. Egen undersøgelsesmetode beskrives. Hos 44 euthyreoide patienter i alderen 8 måneder – 17 år, der var mistænkt for hypothyreoidisme, fandtes en optagelse af J^{131} i gl. thyreoidea efter 24 timers forløb på gennemsnitlig $43,5 \% \pm 1,5$ med en standard deviation på 9,7.

I *kapitel III* behandles tidligere og egne undersøgelser af optagelse af J^{131} hos hypothyreoide patienter. Eget materiale omfatter alle de børn med primær, (thyreogen) hypothyreose, der er undersøgt med den ovennævnte teknik på Dronning Louises Børnehospital de sidste 5 år. Secundære, hypofysært betingede hypothyreoser er ikke medtaget i dette materiale, der efter undersøgelserne deile sig i tre grupper.

Gruppe I: 24 børn med ingen eller meget ringe optagelse af J^{131} over gl. thyreoidea.

Gruppe II: 14 børn med udelukkende ectopisk, sublingval J^{131} -optagelse.

Gruppe III: 18 børn med hypothyreose og struma.

Denne fordeling afviger temmelig meget fra andres materialer. Årsagerne hertil omtales under de enkelte grupper.

Gruppe I omfatter patienter med athyreose og hypoplasia gl. thyreoidea. Disse patienters optagelse af J^{131} ligger langt lavere end de euthyreoides. Der findes ret god overensstemmelse mellem den målte mængde radioaktivitet over gl. thyreoidea, tidspunktet for symptomernes fremkomst og tidspunktet for diagnosen.

Hvad angår den mentale prognose, tyder resultaterne på, at hvis athyreotiske børn (opt. = 0) behandles kraftigt og regelmæssigt fra før 4. levemåned, synes det, som om nogle af dem vil kunne opnå en normal intelligens. Behandles de efter 4. måned, vil chancerne herfor være meget små. Børn med ca. 10 % J^{131} -aktivitet eller mere over gl. thyreoidea diagnosticeres som regel først i løbet af de første leveår, og deres intelligens vil som oftest blive normal.

Af øvrige forhold for patienterne i gruppe I skal nævnes, at der ikke er påvist nogen sammenhæng mellem mødrenes alder og thyreoideamangel hos børnene. Mødrene har med få undtagelser ikke haft thyreoidealidelser i graviditeten. Svangerskab og fødselens forløb har gennemgående været normal, dog med en tendens til »overbårethed«. Positiv toxoplasmosereaktion fandtes hos mor og barn for 2 patienters vedkommende. Betydningen heraf er ikke klarlagt.

Serumcholesterol fandtes som helhed forhøjet hos patienterne i alle tre grupper, hvorimod proteinbundet jod i serum var nedsat, dog med enkelte undtagelser.

Ved sammenligning af fødselslængde, knogle- og tandudvikling hos spæde athyreotide børn i dette materiale, finder man det mærkelige, at knogle- og tandudvikling er prænatalt retarderet, tydende på intrauterin hypothyreose, medens fødselslængden er normal eller endog over normal. Der findes ingen exakte måling angivet i litteraturen for fødselslængden hos athyreotide børn. De faktorer, der kan tænkes at medvirke til det athyreotide fosters vækst, diskuteres. Der peges på den foetale binyrebarks funktion.

Kapitel IV giver først en oversigt over gl. thyreoideas foetale udvikling, specielt descensus fra tungeroden til den endelige placering foran på halsen. Herefter omtales 14 patienter – gruppe II – med ikke palpabelt, sublingvalt ectopisk thyreoideavæv som eneste sted for optagelse af J^{131} . Forfatteren påviste denne foetale misdannelse hos et spædbarn med en lidt larveret form for cong. hypothyreose samtidig med, at det fra anden side blev påvist, at en lignende tilstand kunne være årsagen til nogle af de sene, »aquisite« former for hypothyreose.

Ved herefter systematisk at undersøge alle børn uden J^{131} -optagelse over gl. thyreoideas normale plads, er den nævnte misdannelse fundet hos 14 af 56 i række undersøgte hypothyreosepatienter og må derfor formodes ikke at være nær så sjælden, som man tidligere har antaget. Børn af denne type diagnosticeres som regel noget senere end athyreoserne, og prognosen er tilsvarende bedre. Iøvrigt slutter gruppen sig til gruppe I's hypoplasier af gl. thyreoidea.

Kønsfordelingen for gruppe I og II tilsammen var det sædvanligt opgivne: dobbelt så mange piger som drenge. Ser man imidlertid på tilfældene diagnosti-

cerede før 6 måneders alderen, er fordelingen ens for de to køn, medens der er dobbelt så mange piger som drenge diagnosticerede efter dette tidspunkt. Slår man flere tilsvarende materialer sammen, ser man samme forskel, der synes at være significant indenfor 5 % sandsynlighed.

Kapitel V. Der indledes med en omtale af *gl. thyreoides normale hormonproduktion* og forstyrrelser heri enten som følge af jodmangel (*endemisk kretinisme*) eller forstyrrelser i hormonsyntesen p.gr.a. medfødte enzymdefekter og lignende.

Gruppe III: Der beskrives 18 egne patienter med hypothyreose og struma og gøres blandt andet opmærksom på den udtalte *familiære disposition* og forekomsten af et stort antal (*ca. 1/3*) af *døve/stumme børn* i denne gruppe. Årsagen hertil diskuteres. Børnene i gruppe III er gennemgående ældre ved diagnosen end børnene i gruppe I. Aldersfordeling for alle tre grupper demonstreres.

De forskellige optagelseskurver for J^{131} diskuteres, og de histologiske fund hos nogle strumectomerede patienter i denne gruppe omtales.

Kapitel VI omhandler på basis af litteraturgennemgang hypothyreose som følge af extrathyreoidal enzymdefekt samt hypothyreose som følge af autoimmunisation (Hashimoto's struma).

Kapitel VII omtaler forholdet mellem »simpel« struma og hypothyreose med struma. Egne undersøgelser over familiær disposition, optagelse af J^{131} , indholdet af proteinbundet jod etc. omtales hos 28 euthyreoider børn med struma.

Kapitel VIII drejer sig om røntgenforandringer hos hypothyreoider børn. Der nævnes de typiske epifysære forandringer, »dysgenesier«, i de lange rørknogler og disse funds diagnostiske betydning. Endvidere vises eksempler på en formentlig ikke tidligere beskrevet type euthyreoider børn af hypothyreotisk habitus med »perifer dysostose« i tærne. Børnene er alle fejlagtigt blevet mistænkt for hypothyreose.

Røntgenforandringer i columna beskrives, dels de lokaliserede deformiteter på overgangen mellem lumbal- og thoracalcolumna, dels mere karakteristisk den almindelige retardering af columna. Denne vises at gå nogenlunde parallelt med retarderingen af den perifere knogleudvikling. Hos spæde har forfatteren i 1954 beskrevet en speciel type »dysgenesier« i corpora. Disse fund diskuteres.

Røntgenbilledet af cranium ved hypothyreose, specielt sella turcica's størrelse omtales, og betydningen heraf diskuteres.

Der vises et sjældent tilfælde af tilsyneladende og passerende osteopetrose hos en spæd athyreotiker med samtidigt optrædende, persisterende emailleforandringer i tænderne.

I *kapitel IX* gennemgås egne undersøgelser af tændernes forhold hos hypothyreoider børn. Det fremhæves, at tændernes størrelse, antal og form er normal, hvorimod emailen er hypoplastisk, dysgenetisk. Dette falder i tråd med tidspunktet for *gl. thyreoides foetale funktion*. *Undersøgelse af emaillehypopla-*

siernes forekomst (ca. 80 % hos de undersøgte hypothyroide børn) kan anvendes til et skøn bl.a. over prænatal hypothyreose, idet disse forandringer meget sjældent ses opstå in utero hos normale børn, eller hos børn med andre sygdomme, og forandringerne udslettes ikke under thyreoidinbehandling.

Tandudviklingen er i det hele mindre følsom overfor ændringer i organismens thyreoideastatus, end knoglekærneudviklingen er det. Tilsvarende gælder også overfor andre hormoner, for eksempel kønshormoner og binyrebarkhormoner.

Kapitel X bringer en omtale af tidligere undersøgelser over fostrets J¹³¹-optagelse hos mennesket. Egne undersøgelser konkluderer i, at fostret tager J¹³¹ op i gl. thyreoidea – men ikke i påviselige mængder andre steder – fra ca. 12–14 svangerskabsuge, og at glandlen synes at være temmelig aktiv.

I de afsluttende bemærkninger diskuteres især den tidlige diagnose og mulighederne af genetisk profylakse samt for intrauterin behandling af fostret gennem behandling af moderen.

CASE HISTORIES

GROUP I

1. Case record no. 390/57:

Girl born 15. 12. 50 in Copenhagen. Father aged 42, mother 29 when child was born. No known family history of thyroid disorder. First child. No miscarriages. Birth weight 3500 g, length 52 cm. Admitted when 10 days old to the local hospital where a diagnosis of hypothyroidism was made, and treatment with adequate dosage begun. The parents are very careful, and treatment has been regularly supervised. Physical development has been normal, but mentally the child is slightly backward with an I. Q. of about 90 when tested on successive occasions. The child has difficulty in keeping up at a normal school. Test with I^{131} when aged 6, after being off thyroid medication for 6 weeks, showed no uptake anywhere on the neck. Height and bone development normal for the child's age.

2. Case record no. 1046/58:

Girl born 1. 8. 53 in Copenhagen. Father aged 20, mother 18 when the child was born. No known family history of thyroid disorder. Only child. Birth weight 3500 g, length 53 cm. From about 1 month, or perhaps a little earlier, this child showed symptoms of hypothyroidism. She was treated for a short time when 2 months old, and again from the age of 4 months, and treatment since has been regular and vigorous. At that time the child showed obvious signs of hypothyroidism with pre-natal bone development and epiphyseal dysgeneses. At the age of 2 months the toxoplasmosis reaction was weak positive, 1: 50, in both mother and child. Later, at the age of 4 months, the reaction was still positive in a dilution of 1: 10. There was no other evidence of congenital toxoplasmosis. At the age of 18 months a tumour developed in the mediastinum. Testing at that time with I^{131} revealed no uptake anywhere over the neck or thorax. (Thyroid treatment was being undertaken, however, when this test took place). At operation a thymoma was found, and careful search for thyroid tissue in the normal position in the neck was carried out with negative results. The physical development of the child has been satisfactory, and at the age of 5 years, height, bone development and teeth eruption are normal. The dental enamel shows hypoplasia of intra-uterine origin. Mentally the child is slightly retarded with an I. Q. of 84.

3. Case record no. 918/58:

Boy born 22. 2. 55 in Copenhagen. Father aged 33, mother 27 when the child was born. No known family history of thyroid disorder. Only child. Normal pregnancy and delivery. Birth weight 3100 g, length 52 cm. Since birth he had shown signs of hypothyroidism. Examined at the age of 2 months, at that time untreated. Found severely hypothyroid with physical and mental retardation. The thyroid gland could not be palpated. Bone development was pre-natal, with "marbling" of the bones. In addition there were typical dysgeneses of the epiphyses, and in the spine. The possibility of congenital hypoparathyroidism was considered, but serum calcium, phosphorus and alkaline phosphatase examinations proved normal, and no other signs of hypoparathyroidism were found. The bone changes later disappeared during thyroid medication. Serum cholesterol was 160 mg

per 100 ml and tests with I^{131} showed no uptake over the neck. Treatment has been regular and vigorous since the diagnosis was made. At the age of 4 years he was mentally retarded with an I.Q. of 80 on successive occasions. Physical development has been normal. The dental enamel shows hypoplasia of intrauterine origin, and has a peculiar opaque appearance not seen in any other hypothyroid children examined.

4. *Case record no. 607/58:*

Girl born 1.10.52. Father aged 22, mother 19 when the child was born. No known family history of thyroid disorder. First of two children. Normal pregnancy and delivery. Birth weight ? g, length ? cm. At the age of 2 months the child was found to have severe hypothyroidism, and has since been under regular treatment. Physical development at the age of $5\frac{1}{2}$ was normal, but there was severe mental retardation. Test with I^{131} showed no uptake anywhere over the neck.

5. *Case record no. 51/55:*

Boy born 24.2.40. Father aged (?), mother 23 when the child was born. No known family history of thyroid disorder. Second of two children. Normal pregnancy and delivery. Birth weight 3400 g, length 51 cm. The diagnosis of hypothyroidism was made at the age of 2 months, and regular and vigorous thyroid treatment begun. The child has been seen regularly since. He is now aged 17, and his physical development has been satisfactory. Test with I^{131} after withdrawal of thyroxine for 6 weeks showed no uptake. I.Q. was 55 when he was 3 years old, and his mental development is still very much retarded. He is under the "Care of the mentally defective" for this.

6. *Case record no. 151/58:*

Girl born 19.11.58. Young parents. Fourth child of four. No known family history of thyroid disorder. Normal pregnancy and delivery. Birth weight 3100 g, length 50 cm. When the child was about 2 months old, her length was 53 cm, as compared with a normal 60.5 cm, and her weight was 4.400 kg, as compared with a normal 3.705 kg. She was typically hypothyroid in appearance. The thyroid gland could not be felt. Pulse rate 90, temperature subnormal. Haemoglobin 33 %. Serum cholesterol 155 mg per 100 ml. P. B. I. $0.2 \mu\text{g}$ per 100 ml. E. C. G. showed low voltage peaks. E. E. G. normal. Bone development was pre-natal with absent ossification centres distally in the femur, proximally in the tibia and in the cuboid. The spine seemed to be pre-natal in development with a very marked double contour after 2 months' treatment. The dental development at the age of 4 months was, on X-ray examination, estimated to be—1 month (8 foetal months). Testing with I^{131} showed no uptake over the neck. Since the diagnosis was made, the child has been treated with dessicated thyroid, 100 units per day, and has been seen regularly in the clinic. At 6 months of age the physical development was very satisfactory, and even mental development appeared to be progressing normally as far as could be judged at this early stage of treatment.

7. *Case record no. 609/57:*

Boy born 15.7.54. Father aged 28, mother 25 when the child was born. No known family history of thyroid disorder. First of two children. Normal pregnancy and delivery. Birth weight 3250 g, length 52 cm. When 5 weeks old the child was admitted to the paediatric department because of a stricture of the small intestine. At this time hypothyroidism was diagnosed, and regular treatment instituted. In addition he has an equino varus deformity. Mental and physical development have been satisfactory. Testing with I^{131} when nearly 3 years old showed 10 % uptake over the normal position of the thyroid gland.

8. *Case record no. 489/59:*

Girl born 24. 7. 58. Father aged 36, mother 28 when the child was born. No known family history of thyroid disorder. Second of two children. Normal pregnancy and delivery. Birth weight 4600 g, length 55 cm. Length at the age of 3½ months 58 cm compared with a normal 63 cm, and weight 5.550 kg as compared with a normal 4.650 kg. The child was typically hypothyroid in appearance with cool, dry skin which was coarse in texture with yellowish mottling; pale lips, big tongue, broad, flattened base of the nose, and she was sluggish and sleepy. The thyroid gland could not be felt. Pulse rate 90, temperature subnormal. Haemoglobin 88 %. Serum cholesterol 291 mg per 100 ml. P. B. I. 0.9 µg per 100 ml. E. C. G. showed low voltage peaks. E. E. G. revealed no definite abnormality. X-ray examination showed dysgenesis in the distal epiphyses of the femur and in the cuboid. The proximal tibial epiphyses were missing. Osseous development in the hand was that of a newborn. Spine showed slight signs of double contouring, flattened bodies of the vertebrae with early beaking of the third lumbar vertebra. X-ray showed that dental development at 4 months was between that of full term and two months. Examination with I¹³¹ showed no uptake over the neck. She appears to be developing normally following treatment, as far as can be judged at this early stage.

9. *Case record no. 975/54:*

Boy born 25. 3. 54. Father aged 26, mother 22 when the child was born (first of two). Parents are first cousins. A brother aged 1½ is said to have the same signs as this patient. Normal pregnancy and delivery. Birth weight 3700 g, length 54 cm. The early development of the child was very slow. Hypothyroidism diagnosed at the age of 4 months, and treatment started, but apparently not regularly carried out by the parents. He was again admitted to hospital for re-examination and at the age of 15 months found to be under-dosed. Treatment with higher dosage was instituted, but again neglected when he was discharged home. Re-examined when 2½ years old, when thyroid medication had been discontinued for a month. Rather hypothyroid but height normal. Mentally retarded and sluggish. Bone age showed one year of retardation with epiphysal dysgenesis and changes in the spine. Test with I¹³¹ showed very little activity over the thyroid gland or in any other place.

10. *Case record no. 235/56:*

Girl born 21. 4. 43. Father aged 45, mother 41 when the child was born. No known family history of thyroid disorder. Youngest of 6 children. Normal pregnancy and delivery. Birth weight 3500 g, length (?) cm. Hypothyroidism diagnosed at 5 months following increasing retardation. In spite of vigorous and continuous treatment from the time of diagnosis, she remained severely retarded mentally. Physical development was normal. Test with I¹³¹ when the patient was 13 years old, and in full puberty with a height of 162 cm as compared with a normal 153 cm (after being off thyroid for 4 weeks) showed no activity anywhere over the neck.

11. *Case record no. 113/55:*

Boy born 10. 1. 41. Father aged 33, mother 39 when the child was born. The mother is said to have had "something wrong with her metabolism". She normally takes thyroid, and probably took it during pregnancy. He is the first of two children. Two miscarriages. Birth weight 3200 g, length 48 cm. Admitted at 5 months to the local hospital because of hypothyroidism, since then regularly treated with adequate doses of thyroid. Physical development satisfactory. At one time thought to be slightly deaf, but now seems to hear well without any hearing-aid. Mentally slightly retarded but does well at his job as a petrol-pump attendant. Test with I¹³¹ when he was 14 years showed very decreased uptake over the normal thyroid area and none elsewhere.

12. *Case record no. 330/57:*

Girl born 9.1.55. Father aged 22, mother 20 when the child was born. No known family history of thyroid disorder. Pregnancy and labour normal. Child said to have "a slight yellowish tinge, around the nose only". Only child. Birth weight 3700 g, length 54 cm. Said to be well for the first two months after birth, then loss of appetite, became constipated, with cool, mottled skin, big tongue etc. Admitted to the local hospital when 7 months old, and a diagnosis of hypothyroidism was made. Serum cholesterol 375 mg per 100 ml, P. B. I. 7.0 μ g per 100 ml. Follow-up since being on treatment with thyroid has shown repeatedly high P. B. I. determinations, 10.8 μ g per 100 ml to 13.7 μ g per 100 ml, after thyroid medication had been discontinued for a month. Then became constipated with cool skin, and at the age of 2 years and 2 months her height was 89 cm compared with a normal 88 cm, weight 13.5 kg compared with 12.2 kg normal. X-rays of limbs and spine revealed normal bone development and structure for her age. Test with I^{131} showed very little uptake over the normal thyroid area, and none elsewhere. Mentally retarded, made no attempt to feed herself and did not talk at all.

13. *Case record no. 1859/58:*

Boy born 29.10.55. Father aged 36, mother 35 when the child was born. Only child. No known family history of thyroid disorder. Uterine fibroma was removed between the 2nd and 3rd month of pregnancy, but pregnancy continued uncomplicated otherwise. Delivery by forceps; there was no asphyxia. Birth weight 3500 g, length 51 cm. Admitted to a paediatric department when 10 months old, and at that time she could not sit up alone, and made no attempt to stand. She had no teeth and was severely retarded mentally. Hypothyroidism diagnosed. Height 74 cm as compared with a normal 80 cm. Serum cholesterol 203 mg per 100 ml to 165 mg per 100 ml. P. B. I. 0-4.2 μ g per 100 ml. Toxoplasmosis reaction negative. Bone development severely retarded. The number of bone centres was 3, the normal number being 15 ± 3.5 . Since then treated regularly with 225 units of thyroid per day. Height at the age of 3 years 2 months was 99 cm as compared with a normal 97 cm and weight 16.1 kg as compared with a normal 18.3 kg. Bone age was $4\frac{1}{2}$ years, and dental age $2\frac{1}{2}$ years with hypoplasia of the dental enamel of intra-uterine origin. Mentally severely retarded with an I. Q. of 52. I^{131} test showed no uptake anywhere over the neck.

14. *Case record no. 1606/56:*

Girl born 17.2.54 in Greenland. When 16 months old, hypothyroidism diagnosed. Untreated until then, and at that time a typical example of hypothyroidism with severe physical and mental retardation and probably hearing loss. She did well on treatment with 100 units of thyroid per day, and was referred to a children's home. She was re-admitted after repeated upper respiratory tract infections, then 2 years old, and still physically and mentally backward, and bore the marks of repeated respiratory infections. X-rays of limbs and spine showed pronounced peripheral ring structure, but the bone development corresponded to age. I^{131} test showed no uptake anywhere over the neck after withdrawal of thyroid medication for 6 weeks. The dose was raised to 200 units per day and the child discharged. 8 months later again admitted; some improvement but still severely retarded mentally and physically. Two attempts at implantation of foetal thyroid tissue into the sternomastoid muscle failed, and the patient was discharged on 300 units of thyroid per day. She is now under the "Care of the mentally defective".

15. *Case record no. 758/57:*

Girl born 12.4.48. Father aged 27, mother 25 when the child was born. No known family history of thyroid disorders. Older of two children. Other child normal. Pregnancy and labour normal. No asphyxia. Birth weight 3600 g, height 54 cm. During the 7th to

12th month of life the child developed slowly physically and mentally, being in addition spastic. At the age of 18 months a diagnosis of hypothyroidism was made, and from then on she was treated with thyroid. The dosage was probably too low during the early years of treatment. Her spasticity has also been regularly treated. Progressed well both physically and mentally. Tested with I^{131} at 9 years, and after thyroid had been discontinued for 2 months, showed too low an uptake over the thyroid gland, and no uptake anywhere else on the neck. After a further two months without thyroid medication, her clinical condition did not alter and another I^{131} test again showed a low uptake over the thyroid gland. Mentally the patient is somewhat retarded, with I. Q. 75 at 8 years.

16. *Case record no. 921/56:*

Boy born 30. 5. 48. Father aged 26, mother 23 when the child was born. No known family history of thyroid disorder. Pregnancy and labour normal. Second of 3 children. Labour was difficult, medically induced. The child was asphyxiated for 6 hours, and cyanotic for 4 more days after delivery. Birth weight 3200 g, length 51 cm. Child apparently developed normally for the first year or two. Eruption of the teeth said to be delayed, and at the age of 2 years 8 months hypothyroidism was diagnosed, and treatment started with desiccated thyroid in doses of 150, 300, 400 units per day. Mental and physical development was satisfactory on this regimen. I. Q. at 7 years was 100. I^{131} test when 8 years old showed no activity over the thyroid gland or anywhere else over the neck, after thyroid medication had been discontinued for 3 weeks.

17. *Case record no. 1231/58:*

Girl born 23. 4. 51. Father aged 53, mother 32 when the child was born. No known family history of thyroid disorder. Youngest of 7 children. Pregnancy and labour normal. Birth weight 3500 g, length 50 cm. Child developed slowly, "the slowest of all seven". Walked alone when about 2 years, and started to talk at about 2-3 years. Admitted to hospital twice for unrelated disorders during the first year of life, and hypothyroidism was not diagnosed on either occasion. Again admitted to hospital at 3 years because of a sore throat, and hypothyroidism was then diagnosed. Since been treated continuously with desiccated thyroid, 200 units per day. When $8\frac{1}{2}$ years old, height was 118 cm as compared with a normal 124 cm, and weight 22.7 kg compared with a normal 28.5 kg. Bone structure normal, with a bone age of 6 and a dental age of 6. Spine normal. Mentally slightly retarded with an I. Q. of 77. I^{131} test, after thyroid had been discontinued for 6 weeks, showed no uptake over the thyroid gland or anywhere else on the neck.

18. *Case record no. 280/58:*

Girl born 28. 8. 49. Father aged 21, mother 19 when the child was born. No known family history of thyroid disorder. First of two children. Normal pregnancy and labour. Birth weight 3400 g, length 53 cm. Early development said to have been normal. Started to walk when 12 months old, and to talk when 2-3 years old. Admitted to hospital at 5 years for excessive overweight. Height 102 cm compared with a normal 110 cm, and weight 25.2 kg compared with a normal 16.6 kg, apparently a severe case of simple obesity. She was mentally alert, and cheeks and lips were of a normal colour. Not constipated. Thyroid gland could not be felt. Pulse 60-70, temperature normal. Haemoglobin 106 %. B. M. R. 93, 90, 84, 78, 91, 97 %. X-ray showed her bone development as that of a 3-3 $\frac{1}{2}$ -year-old with slight epiphyseal dysgenesis in the tarsals. Spine was somewhat under-developed and dental development slightly retarded. I. Q. 94 and she gave the impression of rather low intelligence. I^{131} showed about 10 % uptake over the normal thyroid area. Treated with desiccated thyroid, 200 units per day, and later with 400 units per day. The patient has been followed-up for 5 years, and physically and mentally has developed perfectly well. Now alert and doing well at school. Dental

examination when she was 8 years corresponded to her age with hypoplasia of the enamel of early post-natal type (0-10 months).

19. *Case record no. 473/58:*

Boy born 6.12.52. Father aged 31, mother 25 when the child was born. No known family history of thyroid disorder. Normal pregnancy and labour. Breech presentation. No asphyxia. Birth weight 3000 g, length 52 cm. First of two children. Early development normal. Child sat up without support at 6 months, first tooth at 8 months. Walked at 17 months. When 5 years old he was found at the Welfare Clinic to be 11 cm below average for his age (height from symphysis to floor 47 cm, and overall height 101 cm), and he had not grown very much for some time. At the same time he complained of being tired, and had not progressed beyond "baby talk". He was not constipated. He appeared slightly hypothyroid with somewhat dry, coarse skin and peripheral mottling and coldness. Colour of face and lips somewhat pale: nose not flattened. Dental development slightly retarded, corresponding to 4 years with hypoplasia of the enamel of intra-uterine type. Hearing normal. The thyroid gland could not be palpated. Pulse rate 70, temperature normal. Haemoglobin 109 %. Serum cholesterol 247 mg per 100 ml, P.B.I. 5.4 μ g per 100 ml. X-ray showed bone development corresponding to age of 2 years with epiphyseal dysgenesis in the talus, among other places. Spine X-ray showed broad, somewhat flattened vertebrae, and development was far behind the age. Mentally retarded, I.Q. 75, but this was probably the lowest level of achievement. Could remember numbers fairly well but retention was poor, and he was extremely repetitive with retarded speech. Treatment started with thyroid 200 units per day and the child followed-up for 3 months. During that time development was satisfactory. He grew 1 cm per month and bone development reached the age of 2-3 years. His speaking ability improved considerably. He left the country after 3 months' observation so further follow-up has not been possible.

20. *Case record no. 550/59.*

Girl born 3.1.47. Father aged 20, mother 19 when the child was born. No known family history of thyroid disorder. Mother's I.Q. 88. Pregnancy and labour normal. Only child. Birth weight 3100 g, length 51 cm. The patient was in a children's home for the first 18 months of life, apparently considered a Mongol idiot. Since then in various children's homes and institutions. There has been some degree of hearing loss and ability to speak. Six years old when hypothyroidism was first suspected, and since has been on treatment with desiccated thyroid in doses of 50-200 units intermittently, with long periods without medication, apparently because of suspected intolerance to the drug. When 12 years old she was mentally defective to a severe degree, deaf and dumb, hypothyroid, with retarded height, bone and dental development, and hypoplasia of the dental enamel of pre-natal 0-10 months' origin. I^{131} test showed about 10 % uptake over the normal position of the thyroid gland.

21. *Case record no. 274/75:*

Girl born 23.4.45. Father aged 30, mother 25 when the child was born. No known family history of thyroid disorder. Oldest of 3 children. Pregnancy and labour normal. Birth weight 4000 g, length 56 cm. Apparently developed normally for the first 6 months of life, although a tendency to constipation. During the next 6 months growth slowed down and apparently stopped entirely when 3 years old. Mentally there was nothing to note up to the age of 3 years. First admitted to hospital aged 7 because of increasing tiredness and retardation. She was at that time severely hypothyroid with a bone age of 2-3 years, pronounced epiphyseal dysgeneses and dental retardation. Severely backward. Since treated with desiccated thyroid in doses of 200-400 units per day, and physically has developed satisfactorily. There has been marked mental improvement, and she is now one of the brightest in her class for retarded children.

22. *Case record no. 1342/57:*

Girl born 19.12.48. Father aged 33, mother 32 when the child was born. No known family history of thyroid disorder. First of two children. Mother is only 153 cm high. Pregnancy and labour normal. Forceps delivery. No asphyxia. Birth weight 3250 g, length 48 cm. Patient was examined aged 9 because of decrease in the rate of growth, her two-year-younger brother being two cm higher than she was. Apart from this she was normal in every respect, intelligent (I.Q. 121) and top of her school class. She had never had any thyroid treatment. The thyroid gland could just be felt in the normal place but no goitre was found. On X-ray the bone age was $3\frac{1}{2}$ years with epiphyseal dysgenesis. Dental development corresponded to 6 years with hypoplasia of the dental enamel of intrauterine origin. Serum cholesterol was elevated and the P.B.I. was below the normal level. I^{131} test showed about 15 % uptake over the normal position of the thyroid gland, and nothing elsewhere in the neck. She was put on thyroid medication, and development since then has been satisfactory. She has gained 16 cm during the past 18 months while on treatment, compared with 5 cm in the preceding 18 months.

23. *Case record no. 1860/58:*

Boy born 16.5.48 on the Faroe Islands. Mother 34, father 35 when the child was born. No known family history of thyroid disorder. Second of 2 children. Pregnancy and labour normal. Birth weight 4500 g, length 53 cm. Patient now lives in Greenland. Examined aged 10 years for increasing fatigue, lethargy, over-weight and lack of growth. Height at that time was 136 cm compared with a normal 141 cm, weight 41 kg. Haemoglobin 76 %. X-ray of the bones showed development corresponding to 8-9 years with dysgenesis in the patella. P.B.I. $1.7 \mu\text{g}$ per 100 ml. Total cholesterol 725 mg per 100 ml. E.C.G. showed a total AV block which disappeared later. Aged $10\frac{1}{2}$ years, after being on thyroid, 200 units per day for 3 months, he had a slight hypothyroid appearance, with slightly yellow, cool skin and pale lips. Mentally a little sluggish but otherwise normal. The thyroid gland could not be palpated. The circumference of the neck was 30.5 cm against a right wrist 15.5 cm. Dental development corresponded to 8 years with hypoplasia of the enamel of post-natal type 0-10 months. X-ray of the spine showed the vertebrae to be somewhat flattened. I^{131} test, after thyroid medication had been discontinued for 6 weeks, showed about 14 % uptake over the normal position of the thyroid gland, and nothing elsewhere over the neck. The thyroid could not be palpated readily after discontinuing the thyroid medication. Treated with 200 units per day, and followed-up for about a month after discharge from hospital before going home to Greenland. Felt much better, was less tired and had grown $2\frac{1}{2}$ cm in 2 months.

24. *Case record no. 938/59:*

Girl born 26.2.42. Lives with her mother's parents as her mother died when the child was very young. Data on early development inadequate. Seemingly no family history of thyroid disorders. The first of two children, and aged 17 when first seen. Appeared to have developed normally until the age of 12, when found to be too small and too fat. Hypothyroidism diagnosed, and treatment with 400-600 units of desiccated thyroid per day was started. On this regimen she had developed normally both physically and mentally. At the age of 17 withdrawal of thyroid was attempted, but her skin became dry and cool, her hair dull and she complained of tiredness. I^{131} test showed about 12 % uptake over the normal position of the thyroid gland, and none anywhere else over the neck.

GROUP II

25. Case record no. 665/59 (Children's Hospital, Fuglebakken, Copenhagen):

Girl born 20. 6. 59, premature with a weight of 2450 g, length 50 cm. Second of 2 children. During the first 2 months the child was markedly jaundiced, constipated and failed to thrive, and also very "sleepy", and hypothyroidism was suspected. Serum cholesterol was 330 mg per 100 ml and P. B. I. 2.6 μ g per 100 ml. Bone development was pre-natal. Test with I^{131} showed about 12 % uptake over the base of the tongue and about 4 % uptake over the normal position for the thyroid gland. Treatment started when the diagnosis was established.

26. Case record no. 445/54:

Boy born 12. 12. 53. Second of two children. Mother and father both 29 when the child was born. Family history: mother has had goitre since puberty, increasing during pregnancy. She is euthyroid, never been treated for the goitre. Mother's sister also had goitre during puberty. Pregnancy normal. Labour induced medically for post-maturity. No asphyxia. Birth weight 4700 g, length 57 cm. Sluggish since birth with postural instability. Skin cold, dry and mottled; constipated. Feeds slowly. When about 4 months old 62 cms in length compared with a normal 64 cms and 6.9 kg in weight compared with a normal 5.5 kg. Hypothyroid appearance although cheeks and lips were unusually red. Inter-ocular distance was not very much increased and tongue not enlarged. Thyroid gland could not be felt. Mentally he was somewhat slow. Pulse rate 90, temperature sub-normal. Haemoglobin 83 %. Serum cholesterol 247 mg per 100 ml. Toxoplasmosis reaction negative. E. C. G. normal. E. E. G. revealed no definite abnormality. On X-ray, distal ossification centre of the femur very small with dysgenesis, proximal centre of the tibia had developed but that of the cuboid was missing. Spinal development retarded with slight double-contouring. After 2 months' treatment X-ray showed considerable growth of the distal ossification centre of the femur. There was pronounced dysgenesis in the spine and in the talus at that time. I^{131} test at 16 months showed a slight uptake over the base of the tongue, none anywhere else on the neck. Has been treated "sub-toxically" with doses of 200-500 units of thyroid per day, but is still retarded with an I. Q. of 84 at 4 years of age. Physical development has been satisfactory, and examination at 3 $\frac{3}{4}$ years showed a dental age of 3 and a bone age of 4 years. Hypoplasia of the dental enamel of intrauterine origin also found.

27. Case record no. 388/55:

Girl born 6. 8. 54. Father and mother both aged 22 when the child was born. No known family history of thyroid disorders. Pregnancy and labour normal (only child). Birth weight 3200 g, length 49 cm. Constipated since birth, otherwise apparently normal. Early development: at the age of 4-5 months she developed increasing motor inactivity and postural instability. The tongue was enlarged. Admitted to hospital for suspected megacolon at 7 months. Length at that time was 67 cm compared with a normal 69, and weight 8.8 kg compared with a normal 8.7. She appeared moderately hypothyroid. There were no teeth, and the tongue was enlarged. She sat upright with difficulty. She was lively but perhaps rather slow mentally. The thyroid gland could not be palpated. Temperature normal. Haemoglobin 80 %. Serum cholesterol 360 mg per 100 ml. E. E. G. normal. X-ray showed retarded bone development corresponding to 0-3 months. No bone centres in the wrist. The distal ossification centres in the femur and the proximal centres in the tibia were just laid down, but dysgenetic stippling was present. Bone development in the spine was retarded, with a dense zone round the vertebral bodies. Slight kyphosis with deformity of L. II. Test with I^{131} showed slight activity (about 6 % uptake) over the base of the tongue. No uptake elsewhere. Treatment with desiccated thyroid, 200 units per day, was started, and physical development has been satisfactory.

Mentally there has also been some degree of progress. I. Q. was 90 when the child was 3 years old, and both one and two years later the patient appeared to be of normal intelligence, although perhaps a little dull. Dental examination when 3½ years showed a dental age of 3 years with hypoplasia of the enamel of intrauterine type. Bone age was 3½ years.

28. *Case record no. 1190/58:*

Girl born 29. 5. 46. Father 25, and mother 26 when the child was born (first of three, no abortions). No family history of thyroid disorders. Pregnancy and labour normal. Birth weight 4000 g, length 51 cm. Early development: could sit up when 6 months old. Hypothyroidism diagnosed at the age of 14 months at local hospital, and treatment with desiccated thyroid, 100 units per day, started. When 10 years old withdrawal of therapy was attempted, but it was found necessary to institute it again 4 months later because of hypothyroid symptoms, and she continued on 100 units of desiccated thyroid a day, and is said to have had this dosage regularly. When she was 12 years old she complained of tiredness and constipation; she appeared dull mentally, was doing badly at school and not growing. When seen at this time her height was 135 cm, compared with a normal 139. The distance from the symphysis to the floor was 65 cm. Weight 38 kg compared with a normal 29 kg. She appeared to be moderately hypothyroid with stunted growth, rather yellowish and pale skin, and pale lips. She had difficulty in sweating, and puberty had not been reached. Though mentally rather dull she did not appear retarded. The thyroid gland could not be palpated. Pulse rate 60, temperature normal. Blood pressure 100/65. Haemoglobin 93 %. Serum cholesterol 255 mg per 100 ml. E. E. G. normal. X-ray of the bones showed a bone age of 9 with normal structure. Spine normal. Dental age 10 years but the reabsorption of the temporary teeth corresponded to something less than her actual age. Hypoplasia of the enamel of post-natal 0-1 year type was found. I¹³¹ test showed about 6 % uptake over the base of the tongue, and none elsewhere on the neck. Unfortunately, due to a misunderstanding, thyroid medication had not been discontinued prior to this test, so the thyroid dose probably suppressed the uptake, which was thus presumably higher than recorded. The patient was judged to be on too low a dosage, and it was raised to 200 units per day, and later to 300 units per day. During the following year the patient grew about 7 cm, appeared much brighter mentally and did well at school.

29. *Case record no. 1364/58:*

Girl born 20. 7. 45. Father 34, mother 32 when the child was born (third of three). No known family history of thyroid disorders. Pregnancy and labour normal. Birth weight 4000 g, length ?. Apparently normal development during the first year of life apart from rather slow eruption of teeth. At the age of 18 months retardation of growth was noticed, hypothyroidism diagnosed and treatment started with desiccated thyroid, 100 units per day, and maintained since. Assessment at 13 years showed normal mental and physical development. She is bright and is in the first grade of secondary school. I¹³¹ examination showed about 12 % uptake at the base of the tongue, and 4 % over the normal position of the thyroid gland. Dental examination at the age of 13 years 2 months showed a dental age of 12 years, with hypoplasia of the enamel of 0-12 months post-natal type. Bone age was 13 years.

30. *Case record no. 640/57:*

Girl born 10. 12. 47. Father and mother both aged 29 when the child was born. First of two children. No known family history of thyroid disorders. Normal pregnancy and delivery. Birth weight 3700 g. Length 52 cm. Constipated since birth but otherwise said to have developed normally until the age of 8-11 months, when she had whooping-cough. Following this she became physically and mentally retarded, and a diagnosis of hypo-

thyroidism was made at 18 months. At that time bone development corresponded to 3-6 months of age with a typical deformity of the 2nd lumbar vertebra with kyphosis of the spine. She developed well mentally and physically on a dose of desiccated thyroid, 100-200 units per day, and the kyphosis disappeared. She was bright and at the top of her class. Examination with I^{131} when she was 10 years showed 7% uptake over the base of the tongue, and none elsewhere on the neck. Dental examination at the age of 10 years 9 months showed a dental age of 10-11 years with hypoplasia of the enamel of post-natal 0-9 months type. Bone age was 10-11 years.

31. *Case record no. 1173/57:*

Boy born 17.5.47. Father 29, mother 27 when the child was born (third of four). No known family history of thyroid disorders. Early development said to have been normal until one year old. Since then growth has been retarded, and hypothyroidism diagnosed when the child was 18 months old, since treated with desiccated thyroid, 100 units per day. Examined at the age of 10 years when he complained of tiredness and had grown only $1\frac{1}{2}$ cm in the past 6 months. Height 118 cm, as compared with a normal 138 cm, weight 22.6 kg compared with a normal 21.4 kg. Appeared to be extremely hypothyroid with pale lips, and waxy, dry, peeling, cool, mottled skin. Sluggish and quiet but not of abnormally low intelligence. Very constipated and tired. Thyroid medication had been discontinued 3 weeks previously, and the thyroid gland could not be palpated. Dental age was 8 years, and there was hypoplasia of the enamel of post-natal 0-10 months type. Pulse rate 50-60. Temperature normal. Blood pressure 90/60. Haemoglobin 95%. E. E. G. normal. I. Q. 100 and he appeared to be of normal intelligence. X-ray showed bone development in the hand corresponding to 4-4 $\frac{1}{2}$ years. There was pronounced dysgenesis of the patella and navicular bone. Spine slightly retarded with somewhat flattened vertebrae. I^{131} examination showed about 12% uptake over the base of the tongue and none elsewhere. Thyroid dose was raised to 200-400 units per day, and since then development has been satisfactory. The patient grew 8 cm in height in the following year.

32. *Case record no. 1653/57:*

Boy born 15.9.44. Father 27, mother 28 when the child was born (only child). No known family history of thyroid disorders. Pregnancy and labour normal. Birth weight 3000 g, length ?. Early development during the 7th to 12th month, he was somewhat flaccid and retarded in development. Began to sit up at the age of 10-11 months, and began to stand without support at 16 months. Seen by a doctor at the age of 9 months, and thought to have a non-specific motor retardation. When he was one year and 9 months old he was referred because of muscular hypotonia. He was flaccid, sat up alone but could not walk. His tongue was big, hanging out of his mouth; no teeth. Mentally he appeared retarded. Length was 69.5 cm, compared with a normal 80.5 cm, weight 10.95 kg, against a normal 8.2 kg. The thyroid gland could not be felt. Pulse rate 90-120. Temperature subnormal. Haemoglobin 76-78%. Serum cholesterol 295 mg per 100 ml. X-ray showed bone development in the hand corresponding to 0-3 months, and dysgenesis of the epiphyses was found in the tarsus. Psychological examination revealed mental retardation, probably due more to lack of activity than lack of intelligence, and no definite conclusion as to intelligence was drawn at this time. Treatment with desiccated thyroid, 200 units per day, was started and the child followed in the outpatients' clinic, and admitted to hospital several times. Mental and physical development have been satisfactory. A few years later, treatment and follow-up became irregular as the child lived under poor social conditions, his parents were divorced, his mother harassed and working outside. When 5 years old he again became obviously hypothyroid, and treatment was started once more with 300 units per day, but again lapsed. When seen next he was 10 years old, obviously hypothyroid, and had taken his tablets only when he felt he needed them. There had been no treatment at all for the preceding 3 months. He

was very tired. Height 138 cm, compared with normal 156 cm, weight 36.2 kg compared with normal 30.8 kg. Colour of the skin waxy, pale lips and cold extremities. Mentally seemed somewhat sluggish and preoccupied. The thyroid gland could not be palpated. E. E. G. normal. Pulse rate 60-70. Temperature normal. Blood pressure 100/80. Haemoglobin 92 %. Serum cholesterol 348 mg per 100 ml. P. B. I. 1.6 μ g per 100 ml. I. Q. 102. A little slow and sluggish but probably really above average intelligence. X-ray examination showed bone development in the hand corresponding to 11 years. Stippling resembling epiphyseal dysgenesis in the greater and lesser trochanters. Spine showed slight retardation. I^{131} test showed uptake over the base of the tongue, and none elsewhere on the neck. Dental examination showed dental age of 11 years with hypoplasia of the enamel. Treatment again instituted with desiccated thyroid, 200 units per day, and he now develops satisfactorily although has difficulty in keeping up at school and cannot concentrate easily.

33. *Case record no. 1270/57:*

Girl born 22. 5. 54. Father 28, mother 20 when the child was born (only child). No known family history of thyroid disorders. Pregnancy and labour normal. Birth weight 150 g, length 53 cm. Began to sit up at 7-8 months and to stand at 12 months. First tooth at 10 months. Constipated from 3 months when she was weaned. At 21 months hypothyroidism suspected and she was referred to hospital. She had had no treatment previously. Height was 76 cm compared with a normal 84 cm, weight 11.3 kg compared with a normal 9.8 kg. Not typically hypothyroid in appearance. Skin colour normal, with 4 upper and 4 lower teeth. Voice low and grunting, however, like that of a hypothyroid child. There was slight thoraco-lumbar kyphosis and the thyroid gland could not be felt. Pulse rate 80-90. Temperature normal. Haemoglobin 77 %. Serum cholesterol 111 mg per 100 ml. X-ray showed bone development in the hand corresponding to 0-3 months and in the feet to 6-12 months; epiphyseal dysgenesis present. Bone development in the spine retarded with deformity of L. II and a corresponding kyphosis. During treatment with desiccated thyroid a ring structure appeared in the talus and calcaneus among other places. I^{131} examination showed 8 % uptake over the base of the tongue, and none anywhere else. Dental examination at 2 years 10 months showed a dental age of 2 years and hypoplasia of the enamel of intrauterine origin. Since the diagnosis was made, treatment with desiccated thyroid, 100-400 units per day, with satisfactory physical development, and the kyphosis has disappeared. During the first year of treatment there was some doubt whether a normal mental development would be reached but a completely normal level of intelligence was attained by the age of 5 years.

34. *Case record no. 1006/59:*

Boy born 6. 6. 46. Father 42, mother 41 when the child was born (no. 6 of 6). No known family history of thyroid disorders. Child's early development said to have gradually slowed down. At 4 years he could neither stand nor talk. At this time hypothyroidism was diagnosed and treatment started with desiccated thyroid, 300 units per day regularly, and development has been satisfactory. Moderate progress in his school class for the 10-11-year-old children, but particular difficulty in reading. At 13 years his height was 150 cm against a normal 134 cm, weight 42 kg against a normal 39.5 kg. Treatment had been discontinued for 3 weeks. He appeared to be slightly hypothyroid with waxy, dry skin and was mentally rather sluggish. Dental development slightly retarded, thyroid gland could not be palpated. Pulse 50-60. Temperature normal. Blood pressure 115/60. Haemoglobin 102 %. Serum cholesterol 420 mg per 100 ml. P. B. I. 0.4 μ g per 100 ml. X-ray showed bone development corresponding to 12-13 years; the structure was normal. Development of spine normal. An I. Q. of 81 "with difficulty in quick mental reaction; when allowed to take his time gave surprisingly reasonable answers". I^{131} test showed about 7 % uptake over the base of the tongue, and none elsewhere on the neck.

35. Case record no. 567/59:

Girl born 4.3.54. Father 28, mother 32 when the child was born (only child). No known family history of thyroid disorders. Pregnancy and labour normal. Birth weight 3200 gm, length 51 cm. Constipated since early infancy, said to have had an "elephant-like" skin. Began to speak at 12 months and to walk at 19 months. Gradual retardation of growth later, became quiet and had no spontaneous activity up to the age of 4, when the diagnosis of hypothyroidism was made, and treatment with desiccated thyroid 200 units per day begun. Development has been satisfactory since then. I.Q. 110 at the age of 14 years. She is in the secondary school and doing well. Height 152 cm at the age of 14 compared with a normal 160 cm, and weight 52.7 kg compared with a normal 41.25 kg. Slightly hypothyroid appearance. Treatment with thyroid had been discontinued 6 weeks previously. Thyroid gland could not be felt. Pulse rate 60-70. Temperature normal. Haemoglobin 113 %. B. M. R. 71-75 %. X-ray showed bone development corresponding to 13½ years with normal bone structure, and spine was also normal. Dental development corresponded to her age. I¹³¹ examination showed about 5 % uptake over the base of the tongue and none elsewhere on the neck.

36. Case no. 1531/58:

Girl born 13.4.54. Father 28, mother 26 when the child was born (only child). No known family history of thyroid disorders. Normal pregnancy and labour. Birth weight 4050 gm, length 53 cm. Development normal during the first year of life, but after 2 years began to walk with a waddling gait, and showed speech retardation. At that time she was diagnosed as an atypical case of chondrodystrophy, but at the age of 4½ she was recognised as being typically hypothyroid. Height at that time was 90 cm, compared with a normal 110 cm, and bone age was 2-2½ years with typical epiphyseal dysgenesis, and changes in the spine. Serum cholesterol was 336 mg per 100 ml, P. B. I. 0.8 µg per 100 ml. Mentally sluggish, speech backward, I.Q. 83. I¹³¹ examination showed an uptake of 11 % over the base of the tongue, and none elsewhere on the neck. She was put on desiccated thyroid, 200 units per day regularly, and responded well, growing 6 cm during the following 6 months. Speech also improved considerably and intelligence seemed normal. Dental examination at 4½ years showed a dental age of 2½ years with hypoplasia of the enamel of intrauterine origin.

37. Case record no. 1013/57:

Boy born 25.1.51. Father 36, mother 31 when the child was born. No known family history of thyroid disorders. Youngest of 6 children. Normal pregnancy and labour. Birth weight 4200 gm, length 54 cm. Cut his first tooth at about 6 months. Began to sit up at 6 months and to walk at 15 months. Talked at 12 months. Growth and development is said to have slowed down from the age of 3 years, and his appetite became poor. Skin became increasingly pale and waxy; constipated. Hypothyroidism diagnosed 6½ years old. Height at that time was 87 cm compared with a normal 120 cm, the distance from the symphysis to the floor being 36.5 cm. Weight was 14.5 kg compared with a normal 12.3 kg. He appeared to be severely hypothyroid. The skin was waxy, mottled, cool and dry. The lips were colourless. The abdomen was large with an umbilical hernia. Voice was coarse and gruff; he was slow to react and irritable, but did not give the impression of being particularly mentally retarded. Thyroid gland could not be palpated. Extremely constipated. Pulse 80, temperature normal. Blood pressure 100/?. Haemoglobin 80 %. Serum cholesterol 346 mg per 100 ml, P. B. I. 0.2 µg per 100 ml. E. E. G. showed slight to moderate diffuse dysrhythmia with too slow activity. No focal abnormality. I.Q. 97; "very babyish, reserved and without spontaneous activity". Hearing normal, X-ray of hand at 6-12 months showed pronounced dysgeneses in numerous centres. Pronounced retardation of spine development. Dental age 4 years, hypoplasia of the enamel of intrauterine type. I¹³¹ test showed about 15 %, with sublingual uptake as sole site of activity. Treatment started with thyroxine 300 units daily, with regular control since. Development

satisfactory. Patient grew 22 cm in height during the next 21 months. Mentally normal, manages well in school.

38. *Case record no. 1021/56:*

Girl born 29.8.42. Father 28, mother 22 when the child was born (oldest of four children). No known family history of thyroid disorders. Normal pregnancy and labour, though 4 weeks postmature. Birth weight 4100 g, length 56 cm. Early development apparently normal until one year old, then a bilateral pneumonia with high fever, and admitted to hospital. Following this illness, her mother thought she developed slowly. Started walking when two years old, became very quiet and did not play like the other children, and was very sleepy and constipated. Put on weight. When 7 years old was admitted to hospital because of dwarfism, but was not treated. At 8½ years hypothyroidism was diagnosed, and treatment started with desiccated thyroid, 100 units per day. Since then has developed satisfactorily, doing fairly well at school but difficulty with arithmetic. I.Q. at 9 years was 105. Said to have had difficulty in tolerating thyroid medication, and on account of this was admitted to hospital for examination at 14 years. Height 145 cm, compared with a normal 160 cm, and weight 38.2 kg compared with a normal 36 kg. Appeared to be slightly hypothyroid with cool, coarse skin. Eruption of teeth slightly delayed. Seemed moderately intelligent. Puberty had just begun. Pulse around 60, temperature normal. Haemoglobin 99 %. Serum cholesterol 455 mg per 100 ml. B. M. R. 93-99 %, I^{131} test showed an uptake over the tongue of about 70 %, and none elsewhere on the neck.

GROUP III

39. *Case record no. 847/59:*

Boy, born 27.7.46. Father 33, mother 24, when the child was born (second of three). Family history: mother's sister has goitre, untreated. In the father's family two boys are mentally deficient. Other children said to be healthy. Birth weight 4300 gm, length . . . Labour was medically induced and protracted. No asphyxia. When 3 months old admitted to hospital for otitis media, and at the same time hypothyroidism was discovered. Since then has been treated with desiccated thyroid, but irregularly and insufficiently. Repeated attacks of otitis media during infancy, and is now almost totally deaf. Mentally, appears to be retarded. When admitted for examination at the age of 13 years his height was 136 cm compared with a normal 153 cm, he had a bone age of 11 years and a dental age of 11 years. His hearing was considerably impaired, and mentally he appeared to be backward. He had a small, soft and diffuse goitre with a low uptake of I^{131} , after thyroid (400 units per day) had been discontinued for 3 weeks. Serum cholesterol was 358 mg per 100 ml and P. B. I. 2.4 µg per 100 ml.

40. *Case record no. 532/57:*

Girl born 17.9.54. Father 27, mother 24 when the child was born (second of three). Family history: mother has quite a small goitre, resembling that of the patient. Appears to be euthyroid. A five-year-old sister is said to be speech-retarded but otherwise normal. Mother felt unwell during pregnancy. (Her goitre is said not to have increased at this time but the information is not altogether reliable). Labour was induced early but the infant nevertheless appeared to be full-term, birth weight being 3000 gm. No asphyxia. Early development: when 3 months old operated on for hare-lip. After the first 6 months of life became increasingly sluggish and flaccid with cold extremities, and had not begun to cut her teeth. Taken to a doctor when 7 months old because of the symptoms, and was admitted to a paediatric department, where hypothyroidism was diagnosed and treatment begun with desiccated thyroid, 150-160 units. After this she gradually improved.

Cut her first tooth when 12 months old, sat up alone at 12 months, and walked alone at 18–20 months. Became bright and alert, and the small goitre reported present since birth disappeared during treatment with thyroid, but recurred when treatment was discontinued 8 weeks prior to the I^{131} test. Otherwise no other symptoms of hypothyroidism after withdrawal of treatment. When examined at the age of $2\frac{1}{2}$ years her height was 89 cm compared with a normal 91 cm, weight 14.9 kg compared with a normal 12.9 kg. Appeared to be euthyroid and of normal intelligence. Hearing normal. The thyroid gland could be palpated as a soft, well-defined, transversely placed body over the sternal notch. She had 8 upper and 8 lower teeth. Pulse 78, temperature normal. Haemoglobin 85 %. Serum cholesterol 171 mg per 100 ml. P. B. I. $2.0\text{ }\mu\text{g}$ per 100 ml. X-ray showed normal bone development and structure, and spine normal. I^{131} test showed an almost normal curve.

41. *Case record no. 1102/58:*

Girl born 3.5.55. Father 25, mother 22 when the child was born (Second of four children, the last two are twins). Family history: father's mother has been thyroidectomized. Mother has never had goitre, not even during pregnancy. She was carefully observed during the last pregnancy, and the twins have been observed since birth and are euthyroid without goitre. Pregnancy uncomplicated and labour normal. There may have been slight asphyxia. Birth weight 4000 g, length 52 cm. Early development: cut her first tooth when 8 months old, started to sit up when 8 months old and began to walk when 21 months old. Developed very slowly during second year of life, made no attempt to talk and apparently could not hear. Not constipated. Examined at 21 months: length 77 cm compared with a normal 85 cm, weight was 10.4 kg compared with a normal 10.3 kg. Slightly hypotonic with a large abdomen. Slight redness of the cheeks but the skin was starting to go waxy. Lips pale. Four upper and four lower teeth. Could not hear, followed a person with her eyes, but did not reach out for things shown to her. Thyroid gland could be palpated as an elongated soft body, transversely placed over the sternal notch (not previously observed). Pulse 90–100. Temperature subnormal. Haemoglobin 105 %. P. B. I. $0.7\text{ }\mu\text{g}$ per 100 ml. E. E. G. showed a little slow activity in the waking curve. X-ray showed that bone development in the hand corresponded to 9–12 months, with doubtful dysgenesis. The spine showed increased anterior notching of the lower thoracic and upper lumbar vertebrae and flattening of the body of L. III. No other abnormality seen. Test with I^{131} showed a normal uptake over the goitre, the patient being untreated at that time. A dental age of one year with hypoplasia of the enamel of intrauterine type. Treated with desiccated thyroid 200–300 units per day, and has been seen regularly in the out-patient clinic. Has a hearing-aid, lips-reads, and is developing normally mentally. When examined at 4 years her height corresponded to her age.

42. *Case record no. 598/59:*

Girl born 18.6.50. Father 26, mother 24 when the child was born (second of two). Family history: her older brother (case no. 54) has the same disease as the patient. No one else in the family known to have the disease. No deafness in the family. Mother had cysto-pyelitis during the first half of pregnancy, treated with sulpha drugs (preparation?). Birth weight 4500 gm, length 57 cm. Child said to have been retarded physically and mentally. First tooth after she was one year old. Just before she was two years she was found to be extremely hypothyroid and put on treatment with thyroid, 200 units per day, but with some breaks. Appeared to be mentally retarded at that time. She was also deaf and dumb. Admitted to hospital for examination at $2\frac{1}{2}$ years when she had been off treatment for 3 months. Appeared to be hypothyroid and was again put on treatment with desiccated thyroid, 200 units per day, treatment since has been regular. Followed in the out-patients' clinic for $2\frac{1}{2}$ –3 years, and then not seen again until 9 years, when she appeared with her brother. By then euthyroid with a height of 142 cm, normal 134 cm. At this time a soft, small goitre could be palpated, not men-

tioned at previous examinations. X-ray showed normal bone development and structure. Intelligence appeared to be normal. Given I^{131} test but was unfortunately still on treatment at this time, and no activity was recorded over the thyroid gland. Serum cholesterol 240 mg per 100 ml. P.B.I. 6 μ g per 100 ml.

43. *Case record no. 1328/56:*

Boy born 10.2.46. Mother aged 20 when the child was born (second of two). No known family history of thyroid disorders. Older sister healthy. Pregnancy and labour normal. Birth weight 3000 g, length 51 cm. Patient developed normally during the first 6 months of life but mentally and physically retarded since, and has developed a lumbar kyphosis. When examined at the age of two years, appeared to be hypothyroid with severe physical and mental retardation. Has been on regular treatment with thyroid 100–500 units per day since, and has developed physically satisfactorily, kyphosis has disappeared. Mentally backward but hearing is normal. Examined at the age of 10 years, after thyroid treatment had been discontinued for two months, whereupon typical hypothyroid appearance returned. Height 140 cm compared with a normal 141 cm. Bone development corresponded to age and structure was normal. A large, soft and diffuse goitre felt. Serum cholesterol 474 mg per 100 ml., P.B.I. 0.5 μ g per 100 ml. I^{131} test showed abnormal uptake over the thyroid gland.

44. *Case record no. 94/56:*

Boy born 24.11.53. Father 33, mother 25 when the child was born (only child). No known family history of thyroid disorders. Birth weight 3750 g, length 53 cm. Early development: cut first tooth at 4 months, started to sit up at 7–8 months. After 12 months he slowed down mentally and physically. Examined at the age of two years and ten months, still untreated. Height 79 cm compared with a normal 89 cm, weight 10.9 kg compared with normal 10.8 kg. Pronounced hypothyroid, could not walk or talk, and expressed himself by grunting. Cheeks and lips were slightly red but the skin was beginning to go waxy. He had 4 upper and 4 lower teeth, and was not deaf. Extremely constipated. The thyroid gland could be palpated, and was slightly enlarged, diffuse but very soft. Pulse 60–70. Temperature subnormal. Haemoglobin 75 %. E.E.G. showed slight diffuse dysrhythmia with a too slow basal frequency. No focal abnormality. I. Q. of 51, "thought to be probably too low an estimation but he was very slow and clumsy in his behaviour. On the whole he was retarded but in a few accomplishments he corresponded to his age." X-ray examination showed bone development in the hand corresponding to 0–3 months with pronounced epiphyseal dysgenesis in several bone centres. The spine was retarded with deep anterior notching, and deformities of L. II and L. III. The sella was slightly ballooned and enlarged. I^{131} test showed normal uptake over the goitre. Treated with 200 units of desiccated thyroid per day, followed up regularly since in the out-patients' clinic. The goitre disappeared after 3 months' treatment. Physical development has been perfectly satisfactory, also good progress mentally. I. Q. 73: "Surprising progress", but it was thought he could do better. When seen at 6 years seemed to be of normal intelligence, although a bit slow. Dental examination at $3\frac{1}{4}$ years showed dental age of 3 years with no hypoplasia of the enamel. Bone age 4 years.

45. *Case record no. 355/56:*

Girl born 20.12.53. Father 22, mother 22 when the child was born (Second of three). No known family history of thyroid disorders. Normal pregnancy and labour. Birth weight 4000 gm, length 53 cm. Goitre present since birth, but early development seems to have been otherwise normal. Cut her first tooth at the age of 8 months, began to sit up at 8 months, to walk at 20 months and to talk at 18 months. At 18 months showed increasing tiredness and psychomotor retardation. Examined at just a little over 2 years, was at that time untreated. Height 82 cm against a normal 86, and she was only slightly hypothyroid in appearance, her hearing was normal. She appeared to be sluggish

and possibly retarded mentally. The circumference of the neck was 28 cm compared with a wrist circumference of 12 cm. There was considerable diffuse enlargement of the thyroid gland, especially of the lateral lobes, the consistency being soft and uniform. Bone development was retarded, corresponding to 6 months. Serum cholesterol was 186 mg per 100 ml, and P. B. I. 2.25 μ g, 2.50 μ g, 2.60 μ g, 3.75 μ g, 3.04 μ g per 100 ml. I^{131} showed very rapid and high uptake over the thyroid gland, followed by rapid decline. On treatment she developed normally physically, but was retarded mentally with an I. Q. of 73, and in particular her speech was backward.

46. *Case record no. 64/58:*

Boy born 23.5.55. Father 25, mother 24 when the child was born (only child). No family history of thyroid disorders. No miscarriages. Pregnancy and labour normal. Birth weight 4100 g, length 56 cm (?53). Early development: began to sit up at 8 months, cut his first tooth at 11 months, walked at 21 months, talked at 24 months. Constipated since one year old. Admitted to hospital twice during first two years of life, once because of bronchitis and once because of accidental scalding. On admission, no goitre or hypothyroidism noticed. When about 2 years old had difficulty in keeping warm. Was "quieter" than before and moved about less. Examined at 2 years 8 months, at this time untreated. Height was 83 cm, compared with a normal 94 cm, distance from symphysis to the floor being 36 cm, and weight 14 kg compared with a normal 12.4 kg. Typical hypothyroid appearance though of the rather late type. Plump with short legs, waxy skin and pale lips. Voice coarse and grunting, mentally slow. The thyroid gland felt as a diffuse, rather small, soft transverse body over the sternal notch; it had not been noted earlier. Pulse 60-70. Temperature normal. Haemoglobin 96 %. Serum cholesterol 280 mg per 100 ml, P. B. I. 4.5 μ g per 100 ml (3.1-6.1 μ g per 100 ml). E. E. G. showed a normal sleep curve and the waking curve showed no definite abnormality. Psychological examination: I. Q. 87: "severely speech-retarded, and though this test placed him among the backward children, he gave the impression of being of normal intelligence." X-ray showed bone development in the hand of about one year of age with pronounced epiphyseal dysgeneses in the shoulder and the knee. Development of spine retarded with deformation of L. I and L. II, and "double contouring" in the lower thoracic and all lumbar vertebral bodies. Dental examination showed a dental age of 2 years, with hypoplasia of the enamel of intrauterine origin. I^{131} test showed a nearly normal uptake curve. The patient was treated with desiccated thyroid, 200 units per day, and has since been followed up regularly in the out-patients' clinic. He grew 14 cm in the first year of treatment. Mentally he developed correspondingly, and at the age of 14 years is now of normal intelligence but still with a slight speech defect; the spinal defect disappeared after one year of treatment and the goitre disappeared after two months of treatment.

47. *Case record no. 64/59:*

Girl born 23.2.56 in Trondheim, Norway. Father 26, mother 28 when the child was born (older of two children). No known family history of thyroid disorders. The other child healthy. Normal pregnancy and labour. No asphyxia. Birth weight 3600 g, length 53 cm.

Early development: cut her first tooth at 6 months, but development slowed considerably after this. She became "too quiet" and sluggish, did not kick or cry like other children, and was very constipated. Seen by a doctor when 2 years and 9 months old. hypothyroidism diagnosed, treatment with desiccated thyroid, 200 units per day, started. Improved considerably since then. (Goitre not previously noticed). Examined at the age of 3 years and 3 months, still on treatment. At that time 92 cm high, compared with a normal 96 cm, and 15.5 kg compared with a normal 13.9 kg. Appeared to be moderately hypothyroid, hypothyroid proportions with short legs and pale waxy skin. Hair was spiky and coarse, intelligence reduced. She cried a lot and was restless and

constipated during first admission to hospital. Bowel function later normal. Hearing normal. The thyroid gland could not be palpated when she was admitted, but after thyroid had been discontinued for 6 weeks, there was a well-defined transverse goitre, a little thicker than a pencil, over the sternal notch. Pulse 60-70. Temperature normal. Haemoglobin 88 %. Serum cholesterol 256 mg per 100 ml. P. B. I. 6.9 μ g per 100 ml (determinations made the day after thyroid had been discontinued).

I. Q. 66. Memory was poor, and she could not learn. She could not express herself in more than monosyllabic words. Motor development nearly normal. X-ray showed bone development of about 2 years, and epiphysial dysgenesis could be demonstrated in a few places. Otherwise bone structure normal. Spine normal. I^{131} test after treatment had been discontinued for 5 weeks showed a rather low uptake over the goitre. Dental examination showed dental age of 2½ years with hypoplasia of the enamel of intrauterine origin. Treatment started with 200 units per day of dessicated thyroid. Considerable progress over the next 3 months both physically and mentally, and the goitre disappeared.

48. Case record no. 351/58:

Girl born 12. 1. 42. Father 34, mother 31 when the child was born (fourth of five children). Two siblings had died. No known family history of thyroid disorders. Normal pregnancy and labour. Birth weight 3500 g. Early development: this appeared to be normal but the clinical picture was obscured by intercurrent diseases. The diagnosis of hypothyroidism with goitre was made at the age of 3 years. At that time she was definitely retarded. Treated since then with dessicated thyroid in doses of 100 units per day for some years, but the treatment at home is believed to have been intermittent. Dosage later raised to 300-400 units per day. Examined when 16 years old, after thyroid treatment had been discontinued for a month. Height 151 cm, normal 164 cm, bone age 13 years and dental age 15 years. Appeared to be hypothyroid with a rather large, soft, diffuse goitre. Neck circumference was 32 cm and that of the right wrist 14 cm. Seemed very backward mentally. Serum cholesterol 372 mg per 100 ml, P. B. I. 0.4 μ g per 100 ml. I^{131} test showed low uptake over the thyroid gland. Treatment with 600 units per day started, but has not reported for control.

49. Case record no. 516/58:

Girl, born 22. 12. 50. Father 36, mother 38 when the child was born (youngest of three). No known family history of thyroid disorders. Other children healthy. Normal pregnancy and labour. Birth weight 2750 g, length 51 cm.

Early development: sat up at 6 months, walked at 11 months, cut her first tooth at 13 months, and began to talk at 3 years. Diagnosis of hypothyroidism and goitre made at that time, and she was admitted to a paediatric department and has since been treated with dessicated thyroid 175 units per day, and is well. The goitre has decreased in size. Seemed rather restless at the age of 7, and thyroid was discontinued for 6 weeks for the examination to be carried out. She then became more susceptible to cold, more tired and sleepy, and the skin coarsened. Examined at the age of 7 years 3 months, height 117.5 cm compared with a normal 123 cm, weight 21.9 kg, compared with a normal 20.9 kg. Appeared slightly hypothyroid with a waxy, rather puffy skin. Mentally normal with normal hearing. The thyroid gland was enlarged, soft and uniform in consistency, the left lobe larger than the right. Neck circumference was 28 cm compared with 12.5 cm for circumference of the right wrist. Pulse 80. Temperature normal. Haemoglobin 95 %. Blood pressure 90/65. Serum cholesterol 280 mg per 100 ml, P. B. I. 1.4 μ g per 100 ml. E. E. G. showed a normal curve. X-ray showed the bone development to be between 6-7 years without epiphysial dysgenesis. The spine was normal. Dental examination showed a dental age of 6 years with hypoplasia of the enamel of intrauterine origin. Examination with I^{131} showed a high uptake over the goitre.

50. Case record no. 1204/54:

Boy, born 10. 1. 45. Father ?, mother 26 when the child was born (only child). No known family history of thyroid disorders. Normal pregnancy and labour. Birth weight 3600 g, length 53 cm. Apparently normal development during the first year of life, but developed a "thick neck" and a dry skin during the second year. Retarded in growth from the age of 5 years, and goitre became more obvious. Examined when 7 years old, and had at that time well-developed hypothyroidism. Treated with desiccated thyroid 200–300 units per day. During the next year it became apparent that hearing was affected, and he was given a hearing-aid and special schooling was arranged. Still severely retarded mentally (borderline between backward and defective). Treatment was discontinued for about 6 months and he became severely hypothyroid during this time. Examined at the end of this period aged 9 $\frac{3}{4}$ years. P. B. I. was 0.41 μ g per 100 ml, and serum cholesterol 383 mg per 100 ml. I^{131} test showed abnormal uptake over the thyroid gland. Thyroid medication was re-started, and has since been carried on regularly in a dosage of 200–400 units per day. Physically he has made considerable progress and his hearing has improved. Mentally backward but manages everyday life rather well. The goitre is hardly palpable.

51. Case record no. 1570/57:

Boy, born 8. 3. 48. Father 36, mother 33 when the child was born (only child). Family history: mother's sister and her two children have goitre. Normal pregnancy and labour. Birth weight 3150 g, length 54 cm. The boy was born with a goitre. He had several attacks of bilateral otitis media in early infancy, and when about 2 years old was found to be deaf and dumb. Otherwise he appears to have developed normally until the age of 5 $\frac{1}{2}$ years. At that time the goitre compressed the trachea, and was nodular in structure, so thyroidectomy was performed. The patient at that time seemed to be euthyroid with a normal height and bone development. 3 $\frac{1}{2}$ years later the patient attended again, having been without treatment. The goitre had recurred as two small, hard, nodular swellings, and he was definitely hypothyroid. At 9 years and 2 months his height was 126 cm compared with a normal 134 cm, bone age was 6 years and dental age 6 years with hypoplasia of the enamel of pre-natal, 0–10 months, type. P. B. I. 0.9 μ g per 100 ml, serum cholesterol 362 mg per 100 ml. Abnormal uptake of I^{131} over the thyroid gland. Thyroidectomy again performed, and the patient was put on treatment with 200 units of desiccated thyroid per day, and followed-up since. Has developed normally both physically and mentally.

52. Case record no. 661/58:

Boy, born 3. 5. 48. Father 27, mother 26 when the child was born (first of three children). Family history: mother was operated on for goitre aged 16. The other children are healthy. Pregnancy and labour normal. Birth weight 4200 g, length 57 cm.

Early development is said to have been normal. Goitre developed at 5 years, later increasing in size. Examined at 10 years. Height at that time 145 cm compared with a normal 139 cm. Appeared to be euthyroid and mentally normal. Dental development corresponded to his age. No hypoplasia of the enamel. Bone age about 9 years. The apophysis of the calcaneus had not been laid down. Stippling in the patella suggested epiphyseal dysgenesis. Serum cholesterol 240 mg per 100 ml, P. B. I. 2.7 μ g per 100 ml. Circumference of the neck 35 cm compared with that of the right wrist which was 14 cm. Big, rather soft goitre showing diffuse enlargement. A single nodule was palpated in the right lobe. Examination with I^{131} showed a high uptake over the thyroid gland. No effect of potassium thiocyanate. Later on treated for 6 months with desiccated thyroid and during this time the goitre partially decreased, but it is reported that the nodular part of the goitre has been removed. His condition is still good.

53. Case record no. 292/53:

Boy, born 15.10.41. Father 49, mother 29 when the child was born (fifth of six children). Family history: mother's brother is mentally defective, etiology unknown. Otherwise no relevant family history.

The family is of very low socioeconomic standard and contact with the parents is poor. Pregnancy and labour normal. Birth weight 4000 g. During the first year of life he gradually slowed down physically and mentally. Discovered by family doctor to be a mentally defective dwarf at 8 years. Bone development at that time was strongly retarded. Thyroid medication was tried but he was reported not to tolerate it. He was then considered a mentally retarded, chondrodystrophic dwarf. At 12 years again referred to hospital suspected of hypothyroidism, and had then the appearance of a typical infantile hypothyroid. Height was 107 cm compared with a normal 140 cm. A small, fibrous goitre was found which had not been noticed previously. Bone development corresponded to about 1-3 years, with pronounced epiphyseal dysgenesis and retardation in the spine. I.Q. 64. Treated with desiccated thyroid in doses of 200-600 units per day, whereupon the goitre disappeared within a short time. At 12 years, I^{131} test showed only slight activity over the thyroid gland, but the patient was under treatment with thyroid 400 units per day, at the time of the examination. Physical development has since been satisfactory but his mental development is very retarded. I.Q. 60 aged 14. When last seen he was 18 years, and his condition was much the same.

54. Case record no. 599/59:

Boy, born 12.12.46. Father 22, mother 20 when the child was born (no. one of two). Family history: younger sister (case no. 42) has the same disease as the patient. No history of deafness or dumbness in the family. Mother had pyelonephritis during pregnancy and was treated with sulpha drugs (preparation?). Delivery normal. Birth weight 2500 g, length 52 cm. Early development normal. Cut first tooth at 7 months, walked alone at 18 months. Bladder and bowel control. Examined when 6 years old because of his sister's admission to hospital, but nothing abnormal was noted except for deaf-mutism, which had been noted since infancy. From 10 years increasingly tired, could not concentrate at school. Examined at 12½ years when his height was 152 cm compared with a normal 150 cm, and his weight 75 kg compared with a normal 41 kg. At first glance he appeared euthyroid, but the skin was excessively mottled on the extremities. Mentally he appeared to be normal, apart from the fact that he was deaf and dumb. Neck circumference was 34 cm and that of the right wrist 12 cm. The thyroid gland was obviously enlarged, soft and elastic in consistency with a single nodule in the right lobe. The pulse was between 60-70. Temperature normal. Haemoglobin 103 %, P.B.I. 5.1 µg per 100 ml (3.4-7.0 µg per 100 ml). E.C.G. and E.E.G. normal. X-Ray showed a bone development of 9 years. No definite epiphyseal dysgenesis, but bone structure in the patella and calcaneal apophysis somewhat stippled. The vertebral bodies in the spine seemed to be slightly flattened. As in his sister's case, spina bifida occulta was present in L.V. Dental age was 10½ years. No hypoplasia of the enamel was found. Test with I^{131} showed an apparently normal uptake curve over the goitre. The patient was thought to have incipient hypothyroidism and was put on treatment with desiccated thyroid, 200 units per day, and is to be followed-up.

55. Case record no. 1637/58:

Boy, born 11.9.44. Father 27, mother 25 when the child was born (oldest of four). Family history: parents healthy. No goitres. Normal hearing. Mother's mother has a goitre, probably Graves' disease. Pt.'s hearing is impaired. Mother's sister and her daughter have goitre, they are euthyroid. Mother's two brothers have reduced hearing but no goitres. Patient's two years younger sister is healthy. Patient's four years younger brother has hypothyroidism with goitre (55 A). Patient's six years younger sister has hypothyroidism with goitre (55 B). Early development is said to have been normal. He is

said to have had goitre as long as he can remember. When he was 12 years old, sub-total thyroidectomy was performed at a local hospital because of compression of the trachea and suspected Graves' disease. B. M. R. at that time was 117, 121. Microscopy of the goitre showed a picture resembling that of endemic goitre with slight thyrotoxic activity. Six months later the goitre recurred, and during the following years he was increasingly tired. He was breathless on exertion and had an irritating, dry cough. He was again referred for further thyroidectomy when 14 years old. Examination at that time showed the patient to be retarded in growth and development, with a dental and bone development corresponding to an age of 9-10 years, i.e. an age *before* the first operation. Bone structure was normal, and there was no hypoplasia of the dental enamel. Serum cholesterol was 328 mg per 100 ml. P. B. I. 1.7 μ g per 100 ml. Test with I^{131} over the remnants of the thyroid gland showed a normal curve. Instead of being re-thyroidectomized the patient was put on treatment with dessicated thyroid and he grew 9 cm during the following year, the goitre nearly disappeared and the serum cholesterol became normal. P. B. I. 3.0 μ g per 100 ml. He is clever, and is doing well in secondary school.

Århus K.H. børneaf., Case record no. 358 & 359/59:

55 A. A four years younger brother was diagnosed as being hypothyroid when 5 years 3 months old. Height 92.2 cm compared with a normal 107.5 cm. Bone development corresponded to 2 years of age. Sella turcica was observed to be large. P. B. I. 0.8 μ g per 100 ml. Typical hypothyroid, physical and mental retardation corresponding to 4 years of age. Thyroid gland at that time could be palpated but was not enlarged. He has now been on treatment with adequate doses of dessicated thyroid regularly for 5 years, his physical and mental development is now normal, and there is no goitre. P. B. I. 4.1 μ g per 100 ml at his last examination. I^{131} test was not done.

55 B. A six years younger sister is said to have been retarded mentally and physically from the age of 6 months. She did not sit up till 11 months. Diagnosed as a case of hypothyroidism when she was 7 years, her height at that time was 104 cm compared with a normal 121 cm. No goitre present. Bone age was about 2 years of age. P. B. I. 3.0 μ g per 100 ml. Mental development retarded. After 2 years' treatment is physically and mentally normal. The thyroid gland is palpable but not enlarged.

56. Case record no. 95/55:

Girl born 19. 12. 38. Father 44, mother 39 when the child was born (only child). No known family history of thyroid disorders. Pregnancy and labour normal. Birth weight 3000 g, length ?. Early development is said to have been perfectly normal. Walked before 14 months, and talked before 2 years. Later development normal until 11-12 years when growth seemed to be stunted. The patient began to look "well-covered" and slowed down mentally a little. Did well at school, and at the age of 16 years she is in high school (first grade). Puberty is beginning, but menstruation has not started, has been somewhat constipated. On examination at the age of 16 her height was 150 cm, against a normal 164 cm, weight 44 kg against a normal 40 kg. At first sight appeared to be slightly hypothyroid, the skin being coolish with a pale yellowish tinge. Lips and cheeks were of a normal colour, and the expression somewhat oligomimic. Eruption of teeth slightly retarded and irregular. Thyroid gland showed slight diffuse enlargement: the circumference of the neck was 32 cm, that of the wrist 15 cm. Pulse 65. Temperature subnormal. Blood pressure 100/60. Haemoglobin 95 %. B. M. R. 72, 69, 72, 74. X-ray showed the bone development to be around the age of 13 years. No epiphysal dysgeneses found. I^{131} test showed low uptake over the thyroid gland. The examination was repeated some months later, after stimulation with thyrotrophic hormone, and gave the same result. She was then treated with dessicated thyroid 200 units per day, dosage later raised to 400 units per day. This dose, however, was found to be too much and was again reduced to 200, and the patient has developed entirely normally on this, both physically and mentally. The goitre disappeared after a few months' treatment.

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**A LONGITUDINAL STUDY OF
ELECTROCARDIOGRAPHIC INTERVALS
IN HEALTHY CHILDREN**

By

ROBERT W. McCAMMON

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**A LONGITUDINAL STUDY OF ELECTRO-
CARDIOGRAPHIC INTERVALS IN HEALTHY
CHILDREN**

ROBERT W. McCAMMON, M.D.

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UNIVERSITY OF COLORADO SCHOOL OF MEDICINE

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Introduction

Normal standards for the measurements of the various electrocardiographic intervals in children have been published by several workers (1-13) since electrocardiography became a universally employed aid in the diagnosis of cardiac conditions in pediatrics. The fact that there are several authoritative standards which disagree with each other indicates that normality is not yet adequately defined. To compound this disagreement by adding yet another group of "normals" can be justified only if a different point of view is presented. The purpose of this paper is to present data of a nature such that it permits better understanding of the meaning of the measurements in a given individual. Parametric considerations, while necessarily employed to present the group data, are of secondary importance in this report to the developmental aspects of electrocardiographic intervals in individual subjects from infancy to early maturity. Serial measurements in a sufficiently large group of subjects permit reasonable definition of the range of variability that may be expected to occur at any single age. They also make it possible to trace changes that occur in the individual from age to age and to determine what degree of variability can be anticipated within a single person over a span of years. Data derived from longitudinal studies have not been published previously in connection with electrocardiographic interval measurements.

Materials and Methods

The Child Research Council has included periodic electrocardiographic tracings as a part of the longitudinal study of a group of healthy, upper-middle-class Denver children since 1927. Most of the subjects of the present study were enrolled before or at birth and were born after 1930, but 10 were born before 1930 and were enrolled at some age after birth but before 10 years of age. Electrocardiograms were recorded as part of the general physical and physiological studies at the birthday anniversary visits and at quarterly intervals between birthdays. Examinations are more frequent during the first year of life, when the children are seen once a month, and less frequent after the peak of adolescent growth is past, when they are seen twice a year until longitudinal growth is complete. After adult stature is attained, examinations are done annually as appointments can be arranged. An attempt is made to make the appointments as nearly as possible at the time of the birthday and at even quarterly intervals between birthdays. Since this is not always possible, an arbitrary selection of records was made which allowed inclusion in the standards for any given age of all tracings taken not more than 1 week before or 1 week after the age during the first 3 years, not more than 2 weeks before or after the age from 3 years to 10 years, and not more than 1 month before or after the age at ages older than 10 years. Records which did not fit these criteria were not used in establishing the group standards but have been used in presenting the data for individuals. No attempt was made to get an electrocardiogram at each visit, since it was not felt that changes were rapid enough to require such frequent sampling after the first 6 months of life. While

scheduling has varied from time to time over the 33 years of the study, the present plan represents less frequent recording than was usual in the earlier period of the study. For the past 10 years, tracings have been taken on all visits during the first year when the cooperation of the infant permitted, at quarterly intervals during the second and third years, and annually thereafter. Pressures of time and mechanical failures occasionally interfere with getting the tracing, but at least one electrocardiogram per year is available on most of the children from one month of age through adolescence. A Victor instrument was used for the first 26 years, and since 1953 a Cambridge, direct-writing, two-channel instrument¹ has been used. The three standard limb leads were recorded throughout. The material analyzed consisted of strips of record approximately 10 inches long for each lead, selected by the technician as representing a section of the record that was as free from artifacts as possible. All records were made with the subjects lying supine, and as nearly relaxed as possible, but time of day, previous activity and interval from the last meal were not controlled.

A total of 4993 tracings recorded from 214 children were analyzed. All measurements were made by the author. The maximum number of tracings for any one subject was 46 for a young woman who was 28 years and 6 months old at the time of the last tracing, and the minimum number included in the study was 4 records for an infant of 6 months. There were 18 children who had fewer than 10 tracings, 54 who had from 10 to 19, 85 who had between 20 and 29, 51 who had from 30 to 39, and 6 who had more than 40 tracings. All intervals were measured in each complex of the entire strip for each of the 3 leads except where the record was unclear and an accurate measurement could not be made. The standard definitions of the beginning and ending of the intervals were used. Pulse rates were calculated from the records of lead II, and the corrected Q-T intervals were calculated only for this lead. Maximum

¹ Provided for the Child Research Council study by the Colorado Heart Association.

measurements recorded were used throughout in the calculation of standards for the various intervals. The data obtained were so voluminous that illustrations have been limited to lead II for the most part, with only the medians of lead I and III indicated for comparison. The tables appended to the paper include the standards for all three limb leads in more detail than was possible in the illustrations.

The degree of accuracy possible in the measurements demands an effort at definition. Measurements were made to the nearest hundredth of a second, since it was found quite early that attempts to measure even to 0.005 second could not be reproduced with any reliability. Three approaches have been employed in this study to assess the degree of reproducibility of the measurements with the hope and belief that reproducibility and accuracy are correlated. The first and simplest approach was used on approximately one fourth of the records in which the P-S and P-T intervals were measured independently of and at some time later than the standard measurements, and the sums of P-R plus Q-S and of P-R plus Q-T as previously recorded were then compared with these new measurements. The second method was to remeasure approximately 1500 records not less than 5 years after the initial measurements were made and to compare the two sets of readings. The third method was done with the cooperation of 5 successive fellows in pediatrics of the Child Research Council, who measured many of the records obtained since July 1, 1949, independently of the author, allowing comparison of measurements between investigators. The results of all three methods were the same, with slightly more than 85% of the compared measurements being identical and just under 15% showing a variation of not more than 0.01 second. It was often impossible to determine what produced the variation or precisely where the differences arose, even when the records which showed it were identified. Not infrequently either one of the two measurements could be justified. From this it was concluded that a potential

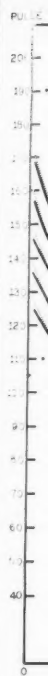


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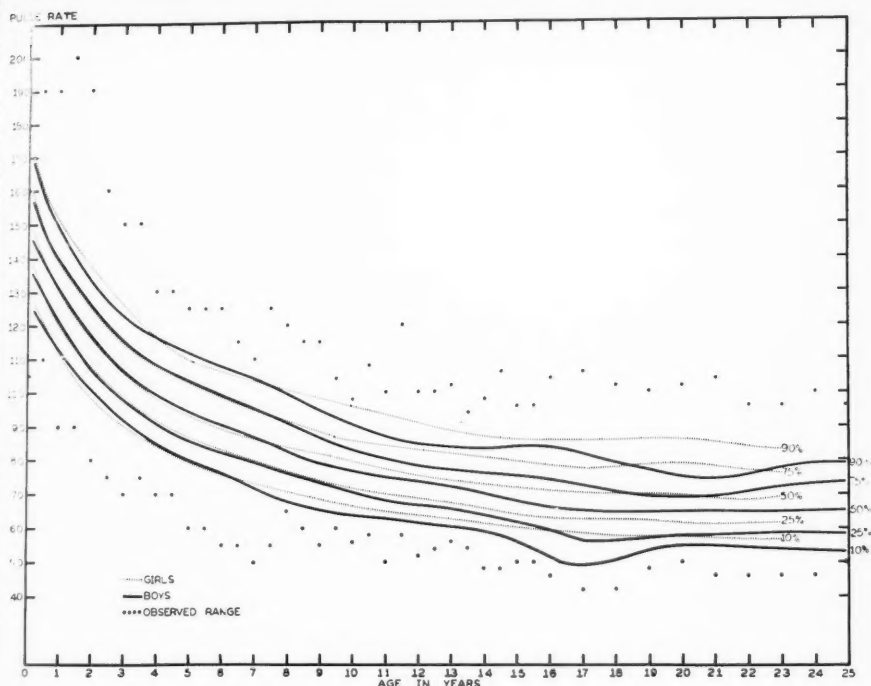


Fig. 1. Percentile pulse rate standards and observed range for boys and girls from 2 months to 25 years of age.

error of ± 0.01 second exists in any measurement, though it will occur only in some 15%. The use of magnification was tried and did not improve the investigator's ability to select end points, which appears to be the major cause of variation. Special calipers were felt to be of assistance by some of the fellows in pediatrics, but in the experience of the author the careful person is greatly slowed by the use of these instruments without corresponding improvement in accuracy.

Percentile norms were computed by the method of cumulative distribution, retaining four decimal places in all interval measurements and two decimals in the pulse rate. These data are recorded in the appended tables. The graphs were drawn by smoothing the percentile lines using the method of three

point moving averages. Small remaining deviations were visually smoothed. The diminished number of cases in the age groups over 20 made it impractical to extend the graphs beyond that age in anything other than the pulse rate.

The Pulse Rate

Fig. 1 represents the pulse rate distribution for boys and girls from 2 months to 25 years of age as determined from lead II of the electrocardiogram. Pulses were calculated to the nearest whole number from the average R-R interval on the available strip. It is evident that the range recorded is not as wide as has been ob-

served before. While these are not basal or sleeping pulses, they represent a range to be expected in children who are lying quietly, and they bear a constant relationship to basal pulses on the same children as published by Iliff & Lee (14). For the most part, each percentile level is about 10 beats faster than the corresponding basal percentile. Records of the pulse during physical examination show a similar but opposite difference from the ECG pulses, running generally ten beats higher. The expected difference between pulse rates for boys and girls is present, but clear separation of the sexes is not apparent until the age of 7 years. Statistical tests for significant difference in the medians for boys and for girls showed no significant differences at any ages except 12 years and 17 years. The absence of statistically significant differences at ages immediately before and immediately after 12 years and 17 years makes the significance at these two ages less impressive. Statistical treatment of the data for other percentile levels was not done because of the few cases involved at these levels.

The pulse rate data are interesting in that this is one of the few measurements which shows a narrower range of variation at adult ages than in infancy. There is a gradual decrease in range of variation which eventually produces essentially a 50% reduction in the range between the 10th percentile and the 90th percentile in the span of the first 25 years of life. This reduction is even more marked if the entire observed range is considered. The expected skewing of the data is present. No adequate explanation could be discovered for the sagging of the 10th percentile and 25th percentile lines for the boys between

14 years and 19 years, while the 75th and 90th percentile lines were bowing upward. No clear-cut relationship could be found between age of adolescence and pulse rate or between known participation in sports and pulse rate during this or other ages. The minimum pulses and those in the 10th percentile range in this age group tended to represent active, vigorous individuals in good physical condition, but since the sample is composed of healthy children, the same may be said for the individuals at and above the 90th percentile.

The upper graphs in Figs. 2 and 3 illustrate the course of the pulse rate during the first 20 years of life for 3 girls and 3 boys. During the first two years at least, there is no tendency for any child to show a clear pattern of pulse rate or to remain within a part of the range. On the contrary, fluctuations throughout the observed range are the rule, occasionally associated with changes in activity which are easily discernible but much more commonly without detectable departure from the "lying quietly" description. At some age over 2 years there does seem to be a tendency for the pulse rate of a child to remain predominantly within a range characteristic of him and less wide than the group range, but this is not a totally stable condition as implied in some previous publications (8). Examples of both short-term but marked deviation from the usual level for one child and of gradual, progressive changes in level for an individual may be seen in the illustrations. These changes were commonly unassociated with recognizable differences in physical state, and so represent pulses under similar conditions within the limits of ordinary observation.

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TABLE 1. *Percentile distribution of pulse (boys).*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
0 1	105	126.33	140.75	152.00	168.25	175.00	185	45
0 2	120	125.10	134.67	145.50	154.00	167.83	185	46
0 3	115	122.50	131.50	141.21	149.50	163.00	185	40
0 4	110	115.50	125.50	137.50	147.17	155.50	175	20
0 5	120	123.25	132.28	137.38	141.12	145.25	165	11
0 6	110	122.50	129.79	137.77	148.50	154.88	185	60
0 9	110	118.90	128.00	135.50	144.25	158.17	200	54
1 0	90	112.30	121.75	132.38	139.15	146.00	190	58
1 3	85	107.67	115.81	125.95	136.75	154.00	185	46
1 6	95	105.90	112.50	121.75	129.07	144.83	180	44
1 9	85	106.30	113.00	118.96	128.36	139.50	155	48
2 0	80	98.50	105.50	115.50	122.64	129.50	155	48
2 3	80	100.50	106.75	113.83	123.62	134.25	165	60
2 6	80	96.83	102.72	110.00	116.93	123.33	160	56
2 9	75	92.00	100.92	110.75	118.16	123.71	145	55
3 0	70	88.17	97.17	102.77	109.88	119.00	135	52
3 3	75	91.40	98.21	108.00	113.98	119.38	150	49
3 6	75	89.50	95.50	101.50	109.39	119.83	140	44
3 9	70	86.17	92.72	99.25	111.33	117.50	160	44
4 0	70	81.00	91.75	98.83	108.00	115.30	130	42
4 3	75	87.70	93.00	100.50	113.00	120.25	130	32
4 6	70	83.50	91.93	97.72	103.36	111.50	120	36
4 9	75	83.12	89.04	97.75	103.89	109.40	120	41
5 0	60	83.50	89.00	97.17	106.75	117.00	125	34
5 3	70	79.17	86.50	90.50	98.62	105.00	115	32
5 6	60	71.50	80.50	88.50	98.00	105.00	135	32
5 9	70	82.33	88.25	95.08	100.75	105.40	110	31
6 0	55	72.00	78.31	87.38	98.25	110.75	120	29
6 3	75	79.00	85.50	91.50	99.25	103.70	110	28
6 6	65	72.40	80.68	86.12	96.75	105.75	125	29
6 9	60	72.83	77.50	85.50	95.50	104.50	110	24
7 0	50	72.50	76.57	85.50	94.67	106.25	110	34
7 3	60	67.50	82.17	90.50	98.00	104.17	115	23
7 6	55	69.75	77.53	84.25	92.79	101.00	110	37
7 9	65	70.75	76.54	81.33	90.08	102.75	115	21
8 0	65	71.00	77.38	83.31	88.31	97.62	100	23
8 3	55	67.70	75.50	84.07	90.50	99.50	115	32
8 6	60	67.75	75.50	81.75	89.50	93.70	100	28
8 9	55	63.50	69.67	78.36	83.00	89.50	105	22
9 0	55	63.33	68.25	79.88	85.92	92.67	105	27
9 3	50	67.33	72.79	78.71	85.92	95.25	105	31
9 6	60	62.30	73.00	76.00	84.83	86.90	94	18
9 9	58	64.90	70.50	76.50	81.83	90.10	94	24
10 0	56	61.90	69.00	77.00	82.00	93.10	98	17
10 3	62	67.60	70.50	75.50	81.50	94.10	98	32
10 6	60	63.90	67.30	75.50	82.50	88.10	96	24
10 9	56	62.90	69.50	78.50	83.83	88.10	102	12
11 0	50	54.70	66.67	72.83	80.00	86.40	90	21
11 3	54	58.40	68.58	72.75	76.38	80.70	88	29
11 6	60	65.10	68.00	77.00	83.00	90.60	92	19
11 9	58	64.90	66.50	74.50	79.50	85.30	88	16

Table 1, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.	Age
12-0	52	58.70	65.62	74.17	76.08	82.30	90	21	5-0
12-3	52	57.70	67.00	72.50	77.00	81.30	88	20	5-3
12-6	54	63.60	67.00	71.75	74.38	77.77	80	21	5-6
12-9	54	56.40	69.25	73.50	79.33	81.60	86	19	5-9
13-0	56	63.40	68.25	73.75	81.00	90.70	102	18	6-0
13-3	44	56.70	60.00	66.50	77.00	81.30	88	22	6-3
13-6	54	61.50	65.83	71.83	75.50	78.50	88	20	6-6
13-9	54	59.30	62.00	71.50	77.50	81.70	94	14	6-9
14-0	48	59.30	61.70	67.50	74.50	85.70	98	23	7-0
14-6	54	62.70	64.88	72.00	79.00	89.90	106	23	7-3
15-0	50	55.10	60.25	67.50	78.75	85.90	92	23	7-6
15-6	50	53.80	56.33	68.00	75.00	81.90	96	23	7-9
16-0	46	49.70	53.50	63.50	72.50	78.10	86	32	8-0
17-0	42	48.10	55.67	63.70	70.00	84.90	96	40	8-3
18-0	42	50.50	55.00	66.50	74.00	76.50	86	30	8-6
19-0	48	54.50	59.50	63.50	68.50	75.50	78	20	8-9
20-0	50	56.55	58.12	64.00	69.67	72.40	84	21	9-0
21-0	54	55.77	57.67	63.50	68.20	73.60	86	19	9-3
22-0	46	53.10	59.25	67.00	77.00	81.90	86	19	9-6
23-0	46	51.10	59.50	62.00	70.50	73.30	84	18	9-9
24-0	46	53.70	59.50	68.50	77.17	79.30	82	16	10-0

TABLE 2. Percentile distribution of pulse (girls).

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.	Age
0-1	105	134.33	141.88	151.44	162.06	177.25	200	63	12-0
0-2	110	131.83	139.50	151.33	163.50	172.50	215	56	12-3
0-3	100	115.25	134.46	143.42	153.31	173.25	220	59	12-6
0-4	110	121.00	129.25	142.00	151.12	159.75	205	23	12-9
0-5	125	129.75	138.62	146.33	157.38	163.75	170	17	13-0
0-6	110	123.90	129.11	138.00	148.00	163.17	190	54	13-3
0-9	110	121.88	126.27	133.00	143.50	154.50	190	52	13-6
1-0	100	116.12	120.36	126.75	136.75	147.75	170	51	13-9
1-3	90	108.20	114.46	129.25	138.75	147.00	190	47	14-0
1-6	90	101.00	113.00	120.50	130.50	145.00	200	52	14-6
1-9	85	100.70	107.38	120.50	129.94	144.50	190	52	15-0
2-0	85	97.00	106.75	115.71	124.56	141.00	190	59	16-0
2-3	85	96.93	104.50	113.00	123.28	132.50	150	60	17-0
2-6	75	94.10	100.50	107.00	115.50	124.50	160	56	18-0
2-9	85	91.40	100.25	108.00	118.21	133.25	155	59	19-0
3-0	85	93.28	99.07	105.95	114.07	128.83	150	60	20-0
3-3	80	91.17	96.61	102.58	111.33	121.00	135	48	21-0
3-6	80	90.50	95.50	103.62	113.83	120.50	150	40	22-0
3-9	75	84.10	91.12	99.14	115.86	121.50	150	46	23-0
4-0	75	83.08	88.42	97.17	103.56	110.90	115	46	24-0
4-3	70	82.08	88.00	101.12	109.88	115.33	130	42	
4-6	75	84.33	87.86	92.69	101.75	114.75	130	33	
4-9	75	81.50	85.50	93.83	103.00	109.00	115	32	

Table 2, cont.

No.	Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
21	5-0	70	76.83	86.00	96.12	102.29	108.50	120	38
22	5-3	75	78.30	83.83	92.50	100.50	106.50	115	28
23	5-6	65	75.83	85.50	90.50	102.50	112.50	135	32
19	5-9	65	74.67	82.25	90.92	98.75	108.00	115	35
18	6-0	65	77.12	85.66	91.00	101.75	112.25	135	33
22	6-3	70	75.17	82.17	88.50	97.17	106.50	125	28
22	6-6	70	76.58	79.25	87.38	95.19	101.33	105	25
14	6-9	70	75.83	83.83	89.39	96.21	99.64	115	32
24	7-0	60	69.50	80.92	86.33	98.00	107.50	120	26
22	7-3	60	72.75	82.11	87.06	92.69	99.00	110	29
22	7-6	65	72.25	76.50	83.83	89.67	103.17	135	24
22	7-9	65	75.00	79.04	85.08	94.88	102.33	110	29
32	8-0	65	69.12	73.75	81.33	90.25	110.75	130	29
40	8-3	60	69.75	77.25	84.88	90.92	97.67	110	27
30	8-6	65	67.20	69.75	81.75	88.25	112.00	125	17
20	8-9	65	71.64	74.43	83.00	89.25	102.50	110	26
21	9-0	60	67.00	75.71	82.00	89.25	99.00	125	29
19	9-3	65	68.62	74.25	79.43	85.25	93.62	100	25
19	9-6	62	65.50	72.00	86.83	91.00	97.50	104	15
16	9-9	64	69.03	75.50	80.50	82.30	86.70	88	18
16	10-0	60	66.30	73.38	77.50	85.75	91.60	98	19
7	10-3	62	65.70	69.50	78.50	87.17	92.90	108	28
7	10-6	58	61.50	68.25	73.50	83.00	89.50	108	15
7	10-9	52	67.50	69.67	72.16	81.00	87.50	98	15
11	11-0	54	57.50	70.00	75.50	91.00	94.00	100	15
11	11-3	66	70.90	73.83	79.50	83.50	87.70	98	24
No.	11-6	58	60.00	64.00	73.50	93.00	100.00	120	15
11	11-9	60	63.90	72.67	75.25	84.00	90.80	92	17
63	12-0	60	67.50	72.00	82.83	87.75	91.50	100	15
56	12-3	62	67.10	69.17	72.50	82.50	91.30	100	16
50	12-6	54	63.50	70.67	76.75	83.25	89.50	100	25
23	12-9	74	75.40	76.75	79.50	82.25	86.70	88	9
17	13-0	60	63.00	64.50	71.50	77.50	82.50	88	20
54	13-3	58	61.30	69.50	73.50	77.50	85.70	90	14
52	13-6	60	61.70	65.50	74.50	83.50	88.90	94	18
51	13-9	60	63.50	68.00	74.83	81.00	87.50	94	15
47	14-0	58	60.40	65.25	75.50	83.00	89.60	92	19
52	14-6	48	59.30	63.50	70.50	76.00	81.70	86	14
52	15-0	50	59.60	64.25	71.50	83.00	91.40	96	31
59	16-0	50	57.50	60.25	69.17	75.50	83.50	94	30
60	17-0	54	60.70	64.67	70.75	76.38	83.20	94	33
56	18-0	48	56.63	61.50	67.50	79.50	85.76	92	22
59	19-0	54	58.57	63.00	71.00	80.00	85.77	90	21
60	20-0	54	58.50	63.50	69.50	82.50	88.50	92	20
48	21-0	46	51.90	61.00	69.50	78.25	89.10	94	17
40	22-0	56	57.10	58.00	63.50	70.00	76.70	78	9
46	23-0	54	63.10	65.75	69.50	81.25	83.90	86	13
46	24-0	58	59.50	61.50	74.50	78.00	88.70	90	10

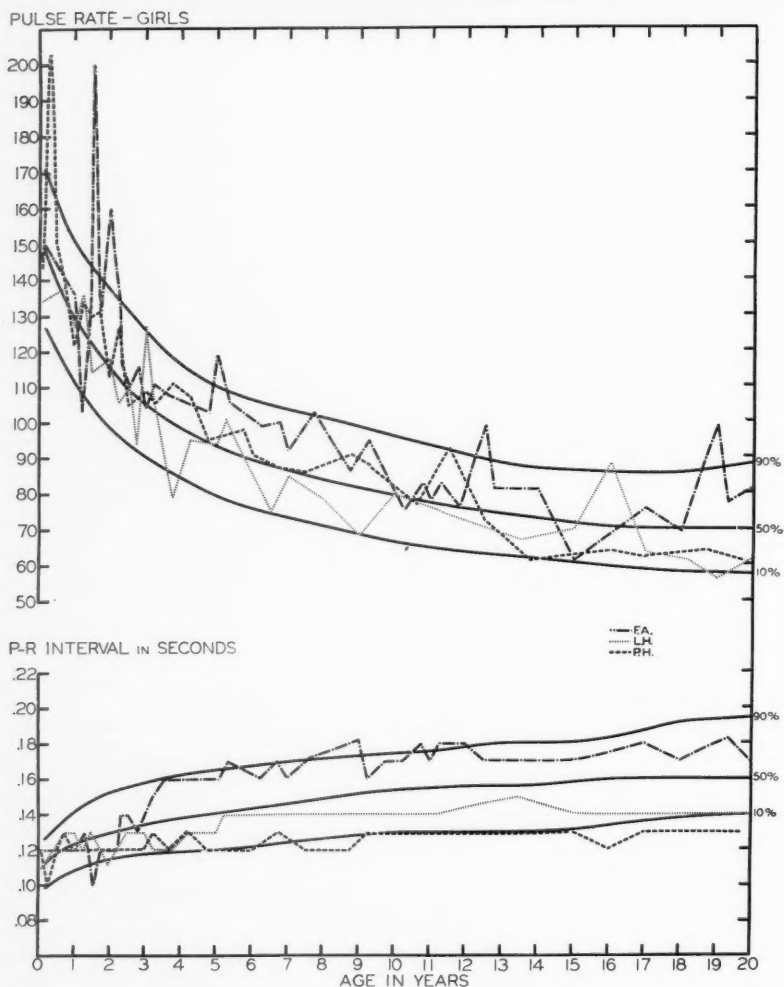


Fig. 2. Pulse rates and P-R interval durations for 3 girls, illustrating the inconstancy of the pulse and the constancy of the P-R duration within the group after age 2 years. Also shown is the lack of inverse relationship between the pulse rate and the P-R duration.

The P-R Interval

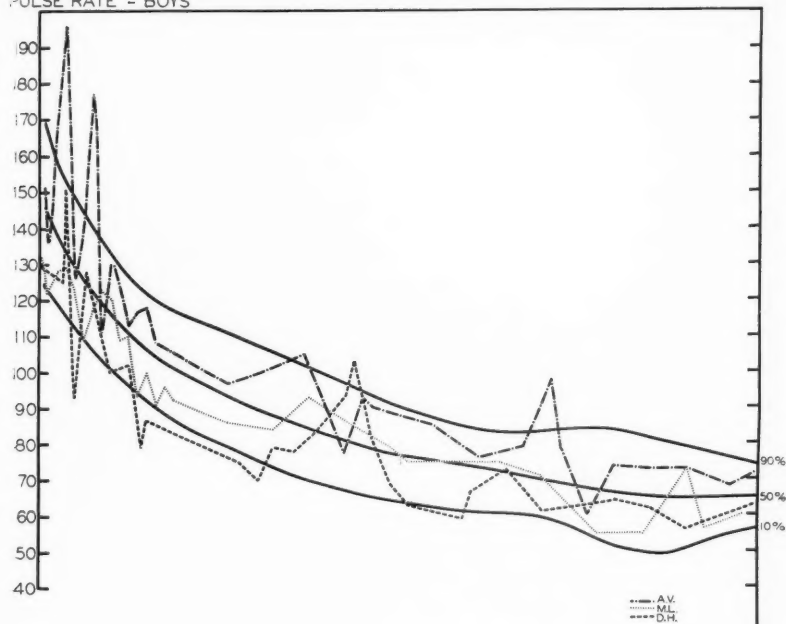
The P-R interval is probably the most widely used interval measurement in pediatric practice. It is also an excellent example of what Kossman terms the "unfortunate and wide-spread practice

of making cardiac rather than electrocardiographic diagnoses from the electrocardiograms" (6). In spite of the general knowledge that innocent murmurs and complaints of leg aches are almost universally present in children at one age or

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PULSE RATE - BOYS



P-R INTERVAL IN SECONDS

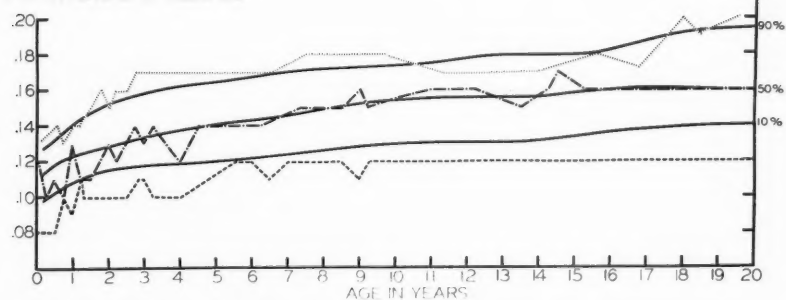


Fig. 3. Pulse rates and P-R interval durations for 3 boys, illustrating the inconstancy of the pulse and the constancy of the P-R duration within the group after age 2 years. Also shown is the lack of inverse relationship between the pulse rate and the P-R duration.

another, a child who offers these complaints on whom an electrocardiogram is recorded in which the P-R interval exceeds the particular physician's definition of maximum healthy duration is very likely to get a diagnosis of rheumatic

heart disease. A similar child whose P-R interval duration falls below this magic level is simply observed by his physician. The difference to the child is quite apparent.

If the total observed range of measure-

ments on healthy children is considered in those publications in which it is recorded, the standards have a remarkable similarity to each other. The major differences arise from the arbitrary selection of the maximum normal duration within the range observed in children selected because they were healthy. The published standards may be divided into three groups on the basis of the method used in establishing them. The first is that group in which there is a simple statement of the observed range and of the average duration (1-3). This is open to the criticism that it offers no idea of the actual distribution of individuals within the range, leaving the impression that the distribution should be regarded as uniform and largely unrelated to age, heart rate and other factors. A second group divides normal from abnormal at the top of the range only, selecting some value as the maximum permissible in health either because it includes the bulk of recorded experience or because it represents some statistical deviation from the mean (4-8). While such a standard recognizes that a few healthy people will exceed the maximum set, it gives no means of recognizing which individuals are healthy in spite of "prolonged" P-R intervals. More particularly, both it and the first type of standards leave the impression that any P-R interval which is shorter than the maximum set is perforce healthy for any individual. The third and most commonly used type of standard is based on the belief that the duration of the P-R interval increases with age and decreases with pulse acceleration (9-13). It is composed of allowable limits for various age brackets, which are further subdivided on the basis

of pulse rate. A major criticism of this type of standard is the lack of objective evidence that processes associated with age alone are not responsible for both the observed slowing of the pulse rate and the concomitant prolongation of the P-R interval. One stated cause of variability is never controlled in any way while testing the importance of the other and opposite cause of variability in the duration of the P-R interval. Studies in which the same individuals have had electrocardiograms before and after exercise thus ruling out change in age while producing changes in pulse rate, have not shown any relationship between pulse rate and duration of the P-R interval (15, 16). A study of a group of adults who had two electrocardiograms 10 years apart found a group tendency for increased pulse rates to be associated with shortened P-R intervals, but there was no uniform tendency for individuals to display the same association (17).

It has been suggested that an isoelectric phase within the early parts of the ECG tracing, especially one which involves the Q wave, may produce falsely long or falsely short P-R interval measurements. The method of White *et al.* (18), to correct the measurements of P-R durations for the influence of possible isoelectric phases was applied to the data of this study. The results of this correction in lead I suggest that the beginning of the P wave in this lead is often isoelectric, since 11.7% of the corrected measurements were longer than the direct measurements from the tracing by 0.02 second or more while 7% of the corrected values were shorter than the direct measurements from the record. In lead III the correspon-

TABLE 3. *Lead I. Percentile distribution of P-R interval.*

Age	10th %	25th %	50th %	75th %	90th %	No.
0-1	0.0887	0.0976	0.1046	0.1163	0.1227	107
0-2	0.0894	0.0977	0.1040	0.1139	0.1218	100
0-3	0.0934	0.0995	0.1088	0.1189	0.1242	96
0-4	0.0895	0.0989	0.1100	0.1192	0.1236	42
0-5	0.0960	0.1008	0.1120	0.1198	0.1234	28
0-6	0.0967	0.1053	0.1160	0.1231	0.1324	115
0-9	0.0982	0.1072	0.1178	0.1254	0.1376	102
1-0	0.1019	0.1100	0.1188	0.1262	0.1372	107
1-3	0.0980	0.1054	0.1180	0.1256	0.1390	90
1-6	0.1024	0.1133	0.1204	0.1294	0.1413	96
1-9	0.1012	0.1141	0.1216	0.1313	0.1422	97
2-0	0.1024	0.1154	0.1218	0.1322	0.1413	104
2-3	0.1077	0.1159	0.1231	0.1343	0.1435	120
2-6	0.1063	0.1169	0.1240	0.1347	0.1484	108
2-9	0.1107	0.1185	0.1264	0.1370	0.1516	113
3-0	0.1144	0.1195	0.1292	0.1413	0.1543	111
3-3	0.1060	0.1159	0.1290	0.1422	0.1586	96
3-6	0.1160	0.1206	0.1323	0.1438	0.1598	84
3-9	0.1154	0.1219	0.1306	0.1421	0.1596	90
4-0	0.1145	0.1202	0.1319	0.1447	0.1570	88
4-3	0.1157	0.1214	0.1318	0.1406	0.1495	72
4-6	0.1126	0.1197	0.1310	0.1425	0.1581	68
4-9	0.1142	0.1230	0.1336	0.1450	0.1607	70
5-0	0.1160	0.1210	0.1318	0.1436	0.1601	71
5-3	0.1165	0.1223	0.1359	0.1481	0.1617	60
5-6	0.1050	0.1208	0.1368	0.1500	0.1600	63
5-9	0.1155	0.1216	0.1345	0.1448	0.1568	66
6-0	0.1192	0.1254	0.1364	0.1515	0.1600	60
6-3	0.1167	0.1234	0.1381	0.1534	0.1637	55
6-6	0.1190	0.1265	0.1377	0.1557	0.1663	53
6-9	0.1169	0.1217	0.1406	0.1550	0.1622	56
7-0	0.1216	0.1298	0.1393	0.1518	0.1631	59
7-3	0.1159	0.1239	0.1395	0.1536	0.1638	56
7-6	0.1192	0.1284	0.1394	0.1562	0.1639	60
7-9	0.1187	0.1270	0.1406	0.1550	0.1640	49
8-0	0.1203	0.1358	0.1478	0.1588	0.1638	52
8-3	0.1175	0.1241	0.1417	0.1600	0.1730	59
8-6	0.1253	0.1343	0.1450	0.1589	0.1690	44
8-9	0.1175	0.1227	0.1407	0.1531	0.1660	47
9-0	0.1261	0.1344	0.1471	0.1562	0.1625	54
9-3	0.1208	0.1290	0.1408	0.1539	0.1743	56
9-6	0.1290	0.1400	0.1494	0.1590	0.1710	32
9-9	0.1196	0.1271	0.1440	0.1605	0.1732	42
10-0	0.1225	0.1320	0.1436	0.1575	0.1650	36
10-3	0.1218	0.1332	0.1445	0.1598	0.1665	59
10-6	0.1232	0.1375	0.1525	0.1606	0.1648	38
10-9	0.1150	0.1283	0.1467	0.1550	0.1650	27
11-0	0.1205	0.1362	0.1445	0.1579	0.1685	36
11-3	0.1278	0.1378	0.1514	0.1634	0.1726	53
11-6	0.1218	0.1305	0.1525	0.1612	0.1680	34
11-9	0.1195	0.1364	0.1467	0.1600	0.1870	31

Table 3, cont.

Age	10th %	25th %	50th %	75th %	90th %	N
12-0	0.1214	0.1325	0.1438	0.1588	0.1648	1
12-3	0.1261	0.1328	0.1558	0.1642	0.1817	1
12-6	0.1253	0.1357	0.1494	0.1600	0.1690	1
12-9	0.1320	0.1410	0.1500	0.1650	0.1810	1
13-0	0.1203	0.1317	0.1500	0.1610	0.1697	1
13-3	0.1270	0.1356	0.1450	0.1644	0.1950	1
13-6	0.1272	0.1356	0.1506	0.1618	0.1768	1
13-9	0.1207	0.1296	0.1438	0.1555	0.1636	1
14-0	0.1181	0.1242	0.1492	0.1611	0.1698	1
14-6	0.1260	0.1370	0.1445	0.1608	0.1685	1
15-0	0.1230	0.1394	0.1538	0.1635	0.1760	1
15-3	0.1270	0.1400	0.1570	0.1630	0.1730	1
16-0	0.1218	0.1360	0.1510	0.1617	0.1694	1
17-0	0.1310	0.1425	0.1556	0.1631	0.1720	1
18-0	0.1275	0.1392	0.1508	0.1619	0.1775	1
19-0	0.1290	0.1383	0.1475	0.1700	0.1830	1
20-0	0.1242	0.1356	0.1572	0.1630	0.1727	1
21-0	0.1222	0.1345	0.1460	0.1602	0.1705	1
22-0	0.1207	0.1342	0.1575	0.1642	0.1793	1
23-0	0.1253	0.1358	0.1512	0.1612	0.1795	1
24-0	0.1265	0.1358	0.1470	0.1662	0.1770	1

ing percentages were 6.25% and 5.6%. Lead II showed closer agreement between the direct and corrected measurements with 3.1% of the corrected measurements longer than the direct measurements and 1% shorter. The corrected P-R interval measurements were not used either in the standards or in the graphs of data for individual children.

Standards for the duration of the P-R interval derived from the data of this study are presented in Fig. 4 and in the appended tables. The medians for leads I and III, superimposed in the figure, represent the usual relationship observed, since the P-R interval in both of these leads was usually somewhat shorter than in lead II at all percentile levels determined. This is in keeping with the previous experience of other investigators. Skewing

of the data is evident, but this becomes marked only after 10 years of age. A statement that the P-R intervals of 0.2 second which were observed are "normal" would be difficult to defend, but they were all observed in one young woman who is now 28 years old and has never had any suggestion of cardiac difficulty in spite of strenuous physical activities in which she habitually participates.

The data for the P-R interval are grouped for boys and girls because standards derived separately for the sexes showed no differences at any age in any lead. As described in a preliminary report (19), the increase with age is half complete by the age of 4 years and is essentially complete by the age of 10 years so far as the group median is concerned. The range from the 10th percentile to the 90th

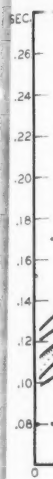


Fig. 4.

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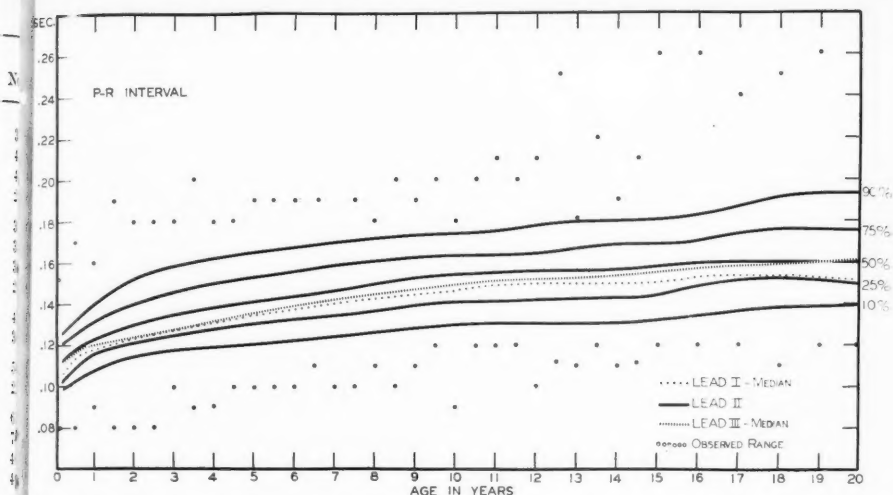


Fig. 4. Percentile standards and observed range of P-R interval duration in healthy subjects from 2 months to 20 years of age.

percentile, representing the middle 80 % of the group, is very narrow at any age, but it doubles from 0.025 second at 2 months to just over 0.05 second at age 20 years, with most of the increase occurring in the first 2 years of life. This central 80 % includes essentially the same range as has been previously published as representing the range of health. The upper ten percent of this group is scattered over a range almost 1.5 times as wide as that occupied by the central 80 % after age 12, and the lowest 10 % of the measurements by age 20 occupies a range equal to that required by the 40 % between the 10th and 50th percentile lines. Thus, the upper and lower deciles combine to cover a range of variation approximately twice as wide as that required for the entire middle 80 %. From this it seems apparent that the distribution of measurements in the upper and lower portions of the ob-

served range is very sparse indeed. This supports the argument that very few healthy individuals will have a P-R interval in excess of 0.18 second, a common upper limit of normal in other standards. It does not, however, seem in any way to support the dependent theories that a P-R interval duration above this level constitutes prima facie evidence of either electrocardiographic or cardiac pathology, and that all P-R interval durations below this level are normal.

During the measurement of serial records of individual children, it became apparent that fluctuations in pulse rate were quite common and sometimes of marked degree and that these were not associated with any change in the P-R interval duration in most instances. Where there were concomitant changes in P-R duration and pulse rate, the P-R seemed equally likely to be either shorter

TABLE 4. *Lead II. Percentile distribution of P-R interval.*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	N	Age
0-1	0.08	0.0954	0.0995	0.1067	0.1150	0.1218	0.15	16	12-0
0-2	0.08	0.0962	0.1013	0.1086	0.1149	0.1250	0.15	16	12-3
0-3	0.08	0.0970	0.1036	0.1143	0.1217	0.1289	0.15	9	12-6
0-4	0.08	0.0922	0.1009	0.1159	0.1216	0.1253	0.14	4	12-9
0-5	0.07	0.0968	0.1054	0.1161	0.1212	0.1244	0.15	2	13-0
0-6	0.08	0.1036	0.1101	0.1182	0.1252	0.1362	0.17	11	13-3
0-9	0.08	0.1040	0.1154	0.1215	0.1303	0.1403	0.16	100	13-6
1-0	0.09	0.1074	0.1159	0.1213	0.1302	0.1412	0.16	16	13-9
1-3	0.08	0.1051	0.1157	0.1220	0.1340	0.1434	0.16	9	14-0
1-6	0.08	0.1108	0.1174	0.1234	0.1363	0.1455	0.19	9	14-6
1-9	0.09	0.1127	0.1184	0.1247	0.1354	0.1463	0.18	9	15-0
2-0	0.08	0.1096	0.1177	0.1243	0.1355	0.1465	0.18	10	15-3
2-3	0.08	0.1158	0.1204	0.1285	0.1382	0.1498	0.17	13	16-0
2-6	0.08	0.1159	0.1215	0.1298	0.1401	0.1540	0.18	11	17-0
2-9	0.10	0.1163	0.1212	0.1295	0.1411	0.1563	0.17	11	18-0
3-0	0.10	0.1165	0.1218	0.1318	0.1430	0.1603	0.18	11	19-0
3-3	0.09	0.1088	0.1201	0.1324	0.1466	0.1613	0.18	9	20-0
3-6	0.09	0.1175	0.1258	0.1375	0.1450	0.1606	0.20	8	21-0
3-9	0.09	0.1177	0.1232	0.1341	0.1465	0.1631	0.18	8	22-0
4-0	0.09	0.1158	0.1211	0.1357	0.1488	0.1565	0.18	8	23-0
4-3	0.10	0.1161	0.1245	0.1333	0.1428	0.1533	0.18	7	24-0
4-6	0.10	0.1176	0.1256	0.1365	0.1454	0.1580	0.18	6	
4-9	0.10	0.1203	0.1298	0.1403	0.1525	0.1640	0.18	7	
5-0	0.10	0.1175	0.1250	0.1350	0.1500	0.1636	0.19	7	
5-3	0.10	0.1207	0.1306	0.1403	0.1506	0.1650	0.19	6	
5-6	0.10	0.1150	0.1225	0.1388	0.1506	0.1616	0.19	6	
5-9	0.10	0.1184	0.1264	0.1386	0.1496	0.1598	0.16	6	
6-0	0.10	0.1206	0.1297	0.1427	0.1535	0.1634	0.19	6	
6-3	0.10	0.1189	0.1271	0.1425	0.1584	0.1660	0.19	5	
6-6	0.11	0.1210	0.1314	0.1419	0.1560	0.1710	0.19	5	0-1
6-9	0.10	0.1172	0.1261	0.1483	0.1596	0.1655	0.20	5	0-2
7-0	0.10	0.1238	0.1312	0.1425	0.1578	0.1690	0.19	6	0-3
7-3	0.11	0.1213	0.1339	0.1446	0.1569	0.1653	0.20	6	0-4
7-6	0.10	0.1214	0.1357	0.1450	0.1588	0.1648	0.19	6	0-5
7-9	0.10	0.1200	0.1319	0.1456	0.1575	0.1700	0.20	4	0-6
8-0	0.11	0.1258	0.1336	0.1500	0.1605	0.1665	0.18	5	0-9
8-3	0.10	0.1220	0.1336	0.1472	0.1621	0.1737	0.20	5	1-0
8-6	0.10	0.1255	0.1381	0.1521	0.1627	0.1777	0.20	4	1-3
8-9	0.10	0.1179	0.1238	0.1419	0.1582	0.1755	0.20	4	1-6
9-0	0.11	0.1323	0.1408	0.1507	0.1594	0.1642	0.19	5	1-9
9-3	0.10	0.1224	0.1365	0.1590	0.1590	0.1710	0.20	5	2-0
9-6	0.12	0.1398	0.1468	0.1571	0.1685	0.1787	0.20	3	2-3
9-9	0.10	0.1264	0.1371	0.1506	0.1665	0.1782	0.20	4	2-6
10-0	0.09	0.1272	0.1375	0.1508	0.1603	0.1655	0.18	4	2-9
10-3	0.11	0.1271	0.1361	0.1480	0.1620	0.1738	0.19	5	3-0
10-6	0.12	0.1276	0.1412	0.1571	0.1640	0.1804	0.20	3	3-3
10-9	0.09	0.1213	0.1425	0.1575	0.1622	0.1745	0.18	5	3-6
11-0	0.12	0.1255	0.1364	0.1478	0.1593	0.1690	0.21	3	3-9
11-3	0.12	0.1290	0.1406	0.1569	0.1641	0.1798	0.24	5	4-0
11-6	0.12	0.1218	0.1369	0.1557	0.1655	0.1736	0.20	3	4-3
11-9	0.10	0.1295	0.1404	0.1525	0.1675	0.1887	0.22	5	4-6

Table

Age

2-4-0

Table 4, cont.

No.	Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
10	12-0	0.10	0.1290	0.1393	0.1490	0.1600	0.1743	0.19	35
10	12-3	0.10	0.1270	0.1390	0.1558	0.1635	0.1900	0.20	42
9	12-6	0.11	0.1210	0.1380	0.1508	0.1605	0.1740	0.25	46
4	12-9	0.12	0.1372	0.1429	0.1575	0.1720	0.1807	0.21	27
2	13-0	0.11	0.1262	0.1375	0.1525	0.1650	0.1727	0.18	39
11	13-3	0.11	0.1300	0.1438	0.1550	0.1740	0.1950	0.20	35
10	13-6	0.12	0.1280	0.1400	0.1550	0.1650	0.1877	0.22	37
10	13-9	0.11	0.1268	0.1365	0.1533	0.1662	0.1808	0.19	29
9	14-0	0.11	0.1266	0.1353	0.1500	0.1614	0.1713	0.19	43
9	14-6	0.11	0.1356	0.1429	0.1550	0.1644	0.1830	0.21	37
9	15-0	0.12	0.1380	0.1473	0.1564	0.1650	0.1857	0.26	54
10	15-3	0.11	0.1270	0.1450	0.1590	0.1650	0.1710	0.20	23
12	16-0	0.12	0.1290	0.1400	0.1573	0.1672	0.1755	0.26	61
11	17-0	0.12	0.1361	0.1456	0.1600	0.1704	0.1860	0.24	76
11	18-0	0.11	0.1340	0.1488	0.1600	0.1733	0.1957	0.25	51
11	19-0	0.12	0.1243	0.1400	0.1570	0.1725	0.1970	0.26	40
8	20-0	0.12	0.1310	0.1440	0.1588	0.1688	0.1830	0.23	41
8	21-0	0.11	0.1347	0.1462	0.1582	0.1658	0.1905	0.23	35
8	22-0	0.12	0.1372	0.1475	0.1620	0.1765	0.1855	0.24	27
8	23-0	0.11	0.1360	0.1525	0.1628	0.1758	0.1973	0.21	29
7	24-0	0.12	0.1360	0.1435	0.1592	0.1794	0.1967	0.20	23

TABLE 5. Lead III. Percentile distribution of P-R interval.

Age	10th %	25th %	50th %	75th %	90th %	No.
0-1	0.0925	0.0981	0.1040	0.1145	0.1217	100
0-2	0.0955	0.0998	0.1073	0.1155	0.1222	93
0-3	0.0956	0.1005	0.1103	0.1201	0.1255	95
0-4	0.0895	0.1038	0.1150	0.1209	0.1245	42
0-5	0.0925	0.1004	0.1155	0.1218	0.1275	24
0-6	0.0992	0.1082	0.1182	0.1246	0.1374	108
0-9	0.1012	0.1138	0.1209	0.1304	0.1404	100
1-0	0.1004	0.1119	0.1199	0.1262	0.1358	99
1-3	0.1051	0.1133	0.1210	0.1298	0.1398	82
1-6	0.1054	0.1163	0.1219	0.1312	0.1446	90
1-9	0.1091	0.1173	0.1234	0.1319	0.1445	93
2-0	0.1023	0.1152	0.1222	0.1334	0.1435	95
2-3	0.1150	0.1185	0.1242	0.1364	0.1440	115
2-6	0.1118	0.1184	0.1249	0.1375	0.1513	106
2-9	0.1156	0.1192	0.1254	0.1369	0.1478	112
3-0	0.1153	0.1198	0.1289	0.1420	0.1591	104
3-3	0.1103	0.1186	0.1293	0.1414	0.1570	92
3-6	0.1159	0.1214	0.1333	0.1441	0.1598	78
3-9	0.1166	0.1209	0.1297	0.1448	0.1621	85
4-0	0.1151	0.1202	0.1303	0.1435	0.1548	82
4-3	0.1172	0.1221	0.1336	0.1438	0.1539	70
4-6	0.1162	0.1225	0.1325	0.1418	0.1538	64
4-9	0.1162	0.1234	0.1338	0.1497	0.1612	66

TABLE 4. *Lead II. Percentile distribution of P-R interval.*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.	Age
0-1	0.08	0.0954	0.0995	0.1067	0.1150	0.1218	0.15	10	12-0
0-2	0.08	0.0962	0.1013	0.1086	0.1149	0.1250	0.15	10	12-3
0-3	0.08	0.0970	0.1036	0.1143	0.1217	0.1289	0.15	9	12-6
0-4	0.08	0.0922	0.1009	0.1159	0.1216	0.1253	0.14	4	12-9
0-5	0.07	0.0968	0.1054	0.1161	0.1212	0.1244	0.15	2	13-0
0-6	0.08	0.1036	0.1101	0.1182	0.1252	0.1362	0.17	11	13-3
0-9	0.08	0.1040	0.1154	0.1215	0.1303	0.1403	0.16	10	13-6
1-0	0.09	0.1074	0.1159	0.1213	0.1302	0.1412	0.16	10	13-9
1-3	0.08	0.1051	0.1157	0.1220	0.1340	0.1434	0.16	9	14-0
1-6	0.08	0.1108	0.1174	0.1234	0.1363	0.1455	0.19	9	14-6
1-9	0.09	0.1127	0.1184	0.1247	0.1354	0.1463	0.18	9	15-0
2-0	0.08	0.1096	0.1177	0.1243	0.1355	0.1465	0.18	10	15-3
2-3	0.08	0.1158	0.1204	0.1285	0.1382	0.1498	0.17	12	16-0
2-6	0.08	0.1159	0.1215	0.1298	0.1401	0.1540	0.18	11	16-0
2-9	0.10	0.1163	0.1212	0.1295	0.1411	0.1563	0.17	11	17-0
3-0	0.10	0.1165	0.1218	0.1318	0.1430	0.1603	0.18	11	18-0
3-3	0.09	0.1088	0.1201	0.1324	0.1466	0.1613	0.18	9	19-0
3-6	0.09	0.1175	0.1258	0.1375	0.1450	0.1606	0.20	8	20-0
3-9	0.09	0.1177	0.1232	0.1341	0.1465	0.1631	0.18	8	21-0
4-0	0.09	0.1158	0.1211	0.1357	0.1488	0.1565	0.18	8	22-0
4-3	0.10	0.1161	0.1245	0.1333	0.1428	0.1533	0.18	7	23-0
4-6	0.10	0.1176	0.1256	0.1365	0.1454	0.1580	0.18	6	24-0
4-9	0.10	0.1203	0.1298	0.1403	0.1525	0.1640	0.18	7	
5-0	0.10	0.1175	0.1250	0.1350	0.1500	0.1636	0.19	7	
5-3	0.10	0.1207	0.1306	0.1403	0.1506	0.1650	0.19	6	
5-6	0.10	0.1150	0.1225	0.1388	0.1506	0.1616	0.19	6	
5-9	0.10	0.1184	0.1264	0.1386	0.1496	0.1598	0.16	6	
6-0	0.10	0.1206	0.1297	0.1427	0.1535	0.1634	0.19	6	
6-3	0.10	0.1189	0.1271	0.1425	0.1584	0.1660	0.19	5	
6-6	0.11	0.1210	0.1314	0.1419	0.1560	0.1710	0.19	5	0-1
6-9	0.10	0.1172	0.1261	0.1483	0.1596	0.1655	0.20	5	0-2
7-0	0.10	0.1238	0.1312	0.1425	0.1578	0.1690	0.19	6	0-3
7-3	0.11	0.1213	0.1339	0.1446	0.1569	0.1653	0.20	5	0-4
7-6	0.10	0.1214	0.1357	0.1450	0.1588	0.1648	0.19	6	0-5
7-9	0.10	0.1200	0.1319	0.1456	0.1575	0.1700	0.20	4	0-6
8-0	0.11	0.1258	0.1336	0.1500	0.1605	0.1665	0.18	5	0-9
8-3	0.10	0.1220	0.1336	0.1472	0.1621	0.1737	0.20	5	1-0
8-6	0.10	0.1255	0.1381	0.1521	0.1627	0.1777	0.20	4	1-3
8-9	0.10	0.1179	0.1238	0.1419	0.1582	0.1755	0.20	4	1-6
9-0	0.11	0.1323	0.1408	0.1507	0.1594	0.1642	0.19	5	1-9
9-3	0.10	0.1224	0.1365	0.1468	0.1590	0.1710	0.20	5	2-0
9-6	0.12	0.1398	0.1468	0.1571	0.1685	0.1787	0.20	5	2-3
9-9	0.10	0.1264	0.1371	0.1506	0.1665	0.1782	0.20	4	2-6
10-0	0.09	0.1272	0.1375	0.1508	0.1603	0.1655	0.18	5	2-9
10-3	0.11	0.1271	0.1361	0.1480	0.1620	0.1738	0.19	5	3-0
10-6	0.12	0.1276	0.1412	0.1571	0.1640	0.1804	0.20	5	3-3
10-9	0.09	0.1213	0.1425	0.1575	0.1622	0.1745	0.18	5	3-6
11-0	0.12	0.1255	0.1364	0.1478	0.1593	0.1690	0.21	5	3-9
11-3	0.12	0.1290	0.1406	0.1569	0.1641	0.1798	0.24	5	4-0
11-6	0.12	0.1218	0.1369	0.1557	0.1655	0.1736	0.20	5	4-3
11-9	0.10	0.1295	0.1404	0.1525	0.1675	0.1887	0.22	5	4-6

Table 4, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
12-0	0.10	0.1290	0.1393	0.1490	0.1600	0.1743	0.19	35
12-3	0.10	0.1270	0.1390	0.1558	0.1635	0.1900	0.20	42
12-6	0.11	0.1210	0.1380	0.1508	0.1605	0.1740	0.25	46
12-9	0.12	0.1372	0.1429	0.1575	0.1720	0.1807	0.21	27
13-0	0.11	0.1262	0.1375	0.1525	0.1650	0.1727	0.18	39
13-3	0.11	0.1300	0.1438	0.1550	0.1740	0.1950	0.20	35
13-6	0.12	0.1280	0.1400	0.1550	0.1650	0.1877	0.22	37
13-9	0.11	0.1268	0.1365	0.1533	0.1662	0.1808	0.19	29
14-0	0.11	0.1266	0.1353	0.1500	0.1614	0.1713	0.19	43
14-6	0.11	0.1356	0.1429	0.1550	0.1644	0.1830	0.21	37
15-0	0.12	0.1380	0.1473	0.1564	0.1650	0.1857	0.26	54
15-3	0.11	0.1270	0.1450	0.1590	0.1650	0.1710	0.20	23
16-0	0.12	0.1290	0.1400	0.1573	0.1672	0.1755	0.26	61
17-0	0.12	0.1361	0.1456	0.1600	0.1704	0.1860	0.24	76
18-0	0.11	0.1340	0.1488	0.1600	0.1733	0.1957	0.25	51
19-0	0.12	0.1243	0.1400	0.1570	0.1725	0.1970	0.26	40
20-0	0.12	0.1310	0.1440	0.1588	0.1688	0.1830	0.23	41
21-0	0.11	0.1347	0.1462	0.1582	0.1658	0.1905	0.23	35
22-0	0.12	0.1372	0.1475	0.1620	0.1765	0.1855	0.24	27
23-0	0.11	0.1360	0.1525	0.1628	0.1758	0.1973	0.21	29
24-0	0.12	0.1360	0.1435	0.1592	0.1794	0.1967	0.20	23

TABLE 5. Lead III. Percentile distribution of P-R interval.

Age	10th %	25th %	50th %	75th %	90th %	No.
0-1	0.0925	0.0981	0.1040	0.1145	0.1217	100
0-2	0.0955	0.0998	0.1073	0.1155	0.1222	93
0-3	0.0956	0.1005	0.1103	0.1201	0.1255	95
0-4	0.0895	0.1038	0.1150	0.1209	0.1245	42
0-5	0.0925	0.1004	0.1155	0.1218	0.1275	24
0-6	0.0992	0.1082	0.1182	0.1246	0.1374	108
0-9	0.1012	0.1138	0.1209	0.1304	0.1404	100
1-0	0.1004	0.1119	0.1199	0.1262	0.1358	99
1-3	0.1051	0.1133	0.1210	0.1298	0.1398	82
1-6	0.1054	0.1163	0.1219	0.1312	0.1446	90
1-9	0.1091	0.1173	0.1234	0.1319	0.1445	93
2-0	0.1023	0.1152	0.1222	0.1334	0.1435	95
2-3	0.1150	0.1185	0.1242	0.1364	0.1440	115
2-6	0.1118	0.1184	0.1249	0.1375	0.1513	106
2-9	0.1156	0.1192	0.1254	0.1369	0.1478	112
3-0	0.1153	0.1198	0.1289	0.1420	0.1591	104
3-3	0.1103	0.1186	0.1293	0.1414	0.1570	92
3-6	0.1159	0.1214	0.1333	0.1441	0.1598	78
3-9	0.1166	0.1209	0.1297	0.1448	0.1621	85
4-0	0.1151	0.1202	0.1303	0.1435	0.1548	82
4-3	0.1172	0.1221	0.1336	0.1438	0.1539	70
4-6	0.1162	0.1225	0.1325	0.1418	0.1538	64
4-9	0.1162	0.1234	0.1338	0.1497	0.1612	66

Table 5, cont.

Age	10th %	25th %	50th %	75th %	90th %	No.
5-0	0.1122	0.1204	0.1330	0.1425	0.1620	67
5-3	0.1181	0.1260	0.1387	0.1514	0.1614	57
5-6	0.1157	0.1223	0.1360	0.1500	0.1620	60
5-9	0.1171	0.1248	0.1379	0.1492	0.1577	50
6-0	0.1180	0.1258	0.1378	0.1516	0.1636	57
6-3	0.1174	0.1240	0.1417	0.1550	0.1632	59
6-6	0.1183	0.1248	0.1388	0.1531	0.1735	59
6-9	0.1169	0.1254	0.1419	0.1575	0.1636	50
7-0	0.1201	0.1292	0.1408	0.1530	0.1615	50
7-3	0.1200	0.1315	0.1421	0.1578	0.1645	50
7-6	0.1210	0.1300	0.1412	0.1570	0.1648	60
7-9	0.1218	0.1300	0.1450	0.1611	0.1703	47
8-0	0.1254	0.1346	0.1425	0.1590	0.1684	48
8-3	0.1208	0.1303	0.1409	0.1554	0.1685	50
8-6	0.1277	0.1400	0.1504	0.1625	0.1734	40
8-9	0.1181	0.1250	0.1388	0.1525	0.1645	40
9-0	0.1280	0.1373	0.1485	0.1587	0.1632	50
9-3	0.1186	0.1317	0.1427	0.1588	0.1780	50
9-6	0.1359	0.1409	0.1538	0.1675	0.1765	30
9-9	0.1210	0.1333	0.1521	0.1638	0.1798	40
10-0	0.1195	0.1366	0.1460	0.1584	0.1639	30
10-3	0.1228	0.1325	0.1421	0.1588	0.1649	50
10-6	0.1258	0.1367	0.1550	0.1627	0.1770	30
10-9	0.1145	0.1319	0.1581	0.1641	0.1787	20
11-0	0.1222	0.1331	0.1431	0.1589	0.1655	30
11-3	0.1270	0.1362	0.1507	0.1617	0.1737	50
11-6	0.1233	0.1406	0.1569	0.1647	0.1738	30
11-9	0.1195	0.1382	0.1492	0.1604	0.1805	30
12-0	0.1270	0.1362	0.1450	0.1590	0.1680	30
12-3	0.1243	0.1342	0.1558	0.1631	0.1860	40
12-6	0.1212	0.1331	0.1519	0.1606	0.1680	40
12-9	0.1357	0.1462	0.1600	0.1720	0.1810	20
13-0	0.1275	0.1388	0.1533	0.1622	0.1775	30
13-3	0.1290	0.1369	0.1450	0.1700	0.1963	30
13-6	0.1210	0.1388	0.1550	0.1667	0.1800	30
13-9	0.1230	0.1378	0.1483	0.1617	0.1790	20
14-0	0.1203	0.1306	0.1480	0.1608	0.1758	30
14-6	0.1363	0.1409	0.1550	0.1621	0.1780	30
15-0	0.1303	0.1419	0.1564	0.1646	0.1785	50
15-3	0.1355	0.1438	0.1592	0.1638	0.1695	20
16-0	0.1227	0.1400	0.1550	0.1657	0.1760	50
17-0	0.1358	0.1436	0.1579	0.1641	0.1760	70
18-0	0.1368	0.1475	0.1578	0.1719	0.1960	40
19-0	0.1356	0.1407	0.1583	0.1800	0.2010	30
20-0	0.1270	0.1392	0.1572	0.1733	0.1837	30
21-0	0.1359	0.1422	0.1567	0.1646	0.1860	30
22-0	0.1347	0.1435	0.1586	0.1705	0.1820	20
23-0	0.1340	0.1442	0.1620	0.1731	0.1860	20
24-0	0.1343	0.1430	0.1594	0.1750	0.1957	20

or longer at the time of pulse acceleration. Just as striking was the apparent lack of proportionate change in the two measurements even when shorter P-R intervals were found in association with more rapid pulse rates. A change of 10 beats per minute in the pulse was just as likely to be associated with a change of 0.01 second in the duration of the P-R interval as was a change of 60-80 beats. In fact, it became clear that pulse rate was remarkably labile, whereas the duration of the P-R interval was the most stable of the measurements being made. Fig. 2 illustrates the measurements of pulse and P-R interval for 3 girls and Fig. 3 for 3 boys. Selection of the children was made on the basis of a P-R interval that fell within the range below 0.18 second and of separation of the P-R intervals into high, central and low within the group at age 10 years. Marked fluctuations of the pulse rate are present for both the girls and the boys, but for the most part all are at levels that can be accepted as usual in that they are within the middle 80 % of the group. Observation supports the lack of relationship between the two measurements, since the P-R intervals show no similar fluctuations. In neither the girls nor the boys is the generally longer P-R interval associated with the generally slower pulse, the median P-R with the median pulse, nor the short P-R with the high pulse.

Separate graphs of the P-R interval measurements in all three limb leads for all the children of the Child Research Council series bore out the impression that the P-R interval is very stable for the individual. In order to evaluate fluctuations that were seen, it was necessary first to take into consideration the presence or

absence of a changing pacemaker, which can cause changes in the P-R interval duration which do not have the same meaning as changes due to other causes. It is recognized that occasionally unmistakable evidence of a changing pacemaker can be present with little or no change in the duration of the P-R interval. However, for the purposes of this study, a changing pacemaker was defined as present when there was a change in the duration of the P-R interval of 0.02 second or more associated with marked change in the configuration of the P wave and with most or all of the change in duration of P-R resulting from changes in the duration of the P wave. Since serial records were available, the additional requirement was imposed that reversion to the previous pattern must occur either within the same tracing or in subsequent tracings. There were a total of 67 children whose records met these criteria, 14 of them only on one occasion and 53 on multiple occasions. Only in rare instances did a change in pacemaker location cause a shift of 0.03 second in the duration of the P-R interval, and in no case did the change exceed 0.03 second. There was no sex difference in frequency. The most common age of occurrence was between 4 and 14 years of age, though in some children it occurred earlier and it was occasionally seen after adolescence. Although a changing pacemaker accounted for some of the fluctuations of 0.02 second that were observed, yet this was by no means adequate to account for all of them.

After elimination of fluctuations due to changing pacemaker, it was evident that the duration of the P-R interval is stable within a given individual, as illustrated in

Figs. 2 and 3. There is an increase in duration with increase in age, but this is of such nature that the child remains consistently at his characteristic level within the group. Fluctuations do occur, as may be seen in the illustrations. During the first two years of life there is much more fluctuation and often a child shifts from one level to another during this period. This is the same age period during which rapid expansion of the group range is taking place. It is tempting to speculate from this that whatever forces are responsible for regulation of the duration of the P-R interval do not attain mature function until about 2 years of age. After that age, however, a fluctuation from one record to another within any span of a single year which exceeded 0.02 second was not observed except in four individuals: one during each of three acute attacks of classical rheumatic fever with rheumatic heart disease, one during a period of convalescence from scarlet fever, one during a long series of repeated respiratory attacks of unknown etiology, and one in a girl at the time of her menarche. The first three showed a return to previous levels within the group with recovery from their illnesses. The girl remained at her new high level.

The clinical importance of this stability of the P-R interval for the individual is apparent. The fact that three of the four individuals who showed fluctuations within the span of a year which exceeded 0.02 second had either classical rheumatic disease or conditions associated with streptococcal infection supports the concept that changes of this magnitude would be more suggestive of disease involving cardiac conduction than would any

single measurement within the observed range up to 0.26 second. The added observation that changes associated with disease occurred simultaneously in all three leads, in the same direction and in approximately the same amount, while casual changes in duration unassociated with disease usually were present in only one lead with the other two showing either no change or even an opposite change, also helps to separate innocent fluctuation from that associated with carditis. In the acute phases of an illness compatible with rheumatic fever, an increase in the P-R duration of 0.03 second over a previously established healthy measurement would be supporting evidence for a diagnosis of carditis. In the absence of a known healthy level, a change of 0.03 second or more in either direction would strongly suggest that the longer interval was abnormally prolonged for that individual. It is also emphasized that children such as P. H. and D. H. in Figs. 2 and 3 could have as much as 0.02 second increase in their P-R interval durations associated with carditis and still be at or below the limit of 0.18 second.

Previous work (20) has indicated that fairly wide fluctuations occur in the duration of the P-R interval in children who have long P-R intervals in the absence of heart disease as well as those who have inactive rheumatic heart disease. In spite of the observation that none of this group showed fluctuations of more than 0.02 second in tracings taken within any single year, there was clearly more fluctuation in the duration of those P-R intervals which fell at or above the 90th percentile than in intervals which fell near the median, while intervals at or below the 10th per-

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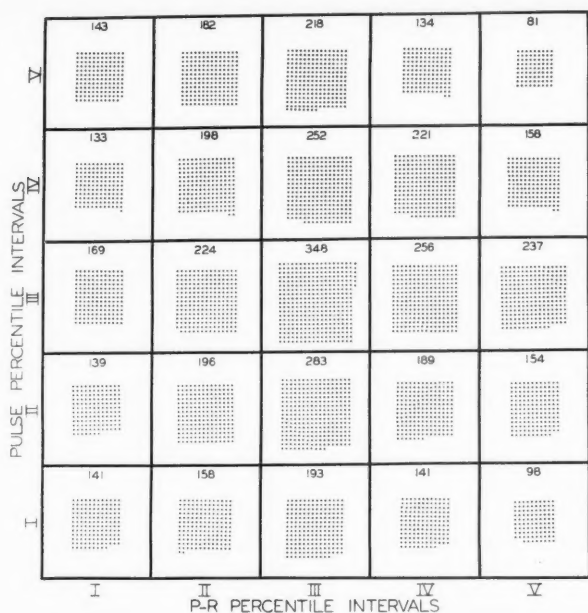


Fig. 5. Scattergram of P-R percentile intervals against pulse percentile intervals showing absence of any line of increased density of dots resulting from dependence of P-R duration on pulse rate.

centile showed both less fluctuation and less change with age than intervals at any other level.

The apparent lack of relationship between pulse rate and the duration of the P-R interval in the individual led to a further investigation of the relationship of these two measurements within the group. Since processes associated with aging seemed to produce an increase in the duration of the P-R interval and a slowing of the pulse, it was felt necessary to rule out the influence of age on the measurements as completely as possible. This was accomplished by a five fold division of the pulse rate and P-R interval duration data such that all measurements that fell between the observed minimum and the 17.5th percentile level were in interval I,

those above 17.5th percentile to 37.5th percentile in interval II, those above 37.5th percentile to 62.5th percentile in interval III, those above 62.5th percentile to 82.5th percentile in interval IV, and those from 82.5th percentile to the observed maximum in interval V. Thus, while the absolute measurements for percentile interval V of the pulse rate changed from the range of 165 to 190 at age 2 months to a range of 87 to 107 at age 25, they were grouped as interval V in both instances. If the concept is correct that increasing pulse rates cause shortening of the P-R interval, one would expect a scattergram of the percentile intervals of pulse against the percentile intervals of P-R duration to show a clear diagonal density of points when the data were

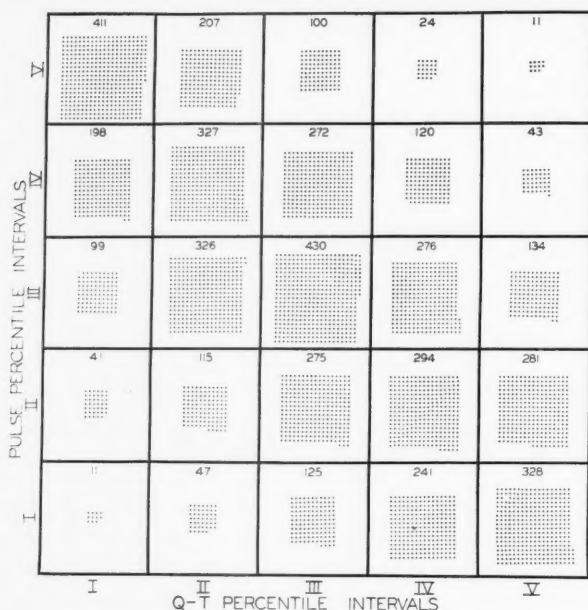


Fig. 6. Scattergram of Q-T percentile intervals against pulse percentile intervals showing diagonal line of density of dots resulting from dependence of Q-T duration on pulse rate.

plotted. Fig. 5, however, demonstrates that no such central trend is apparent, supporting the conclusion gained from the data on separate individuals that there is no influence of pulse rate on the duration of the P-R interval.

As a demonstration that this graphic approach does result in a grouping of the points along a central diagonal when an inverse relationship exists, the Q-T interval data were treated in the same manner. Fig. 6 illustrates the result of graphing percentile intervals of Q-T duration against percentile intervals of pulse rate. There is a clear central concentration of the data along a diagonal line together with remarkable symmetry of the distribution on the two sides of the diagonal. The data presented in Figs. 5 and 6 were

examined further by the staff biostatistician of the Child Research Council. Because correlation coefficients have been used before in testing the relationship between pulse rate and P-R duration, this technique was employed first. For the pulse rate: P-R data, the coefficient of correlation was minus 0.01, indicating a complete lack of linear correlation. For the Q-T: pulse rate data the coefficient of correlation was minus 0.59, indicating some straight-line relationship but supporting the previously published belief that pulse rate is not the only mechanism involved in controlling the length of the Q-T interval (21).

A more logical method of analysis of data in the form represented in the figures is the chi-square test for dependence. This

was used for the pulse rate: P-R data, giving chi-square of 60.6, meaning that the probability of independence of pulse and P-R interval duration is less than 0.00001. In the process of determining the coefficient of correlation it became apparent that the pulse rate: P-R interval dependence is U-shaped rather than straight line in character, which is readily seen from the scattergram. This results from a tendency for both the relatively very rapid and the relatively very slow pulses to be associated with the short P-R intervals. This in turn leads to the speculation that the dependence found between the pulse rate and the duration of the P-R interval is not direct and bifactorial but is probably a result of dependence of both these measurements on some factor or factors not recognized or considered.

Previous work reporting no significant change in P-R interval duration with pulse acceleration from exercise was repeated with a group of 26 children. Exercise was carried out with a bicycle ergometer, adjusting the friction load so that each subject did $\pm 5\%$ of the work he would have done on a Harvard Step Test. Pre-exercise records were made for comparison with the post-exercise tracings taken at one minute after exercise and repeated each minute for five minutes. Pulses of 180 to 200 are quite frequent after this exercise, and in such an electrocardiogram the P wave of one complex overrides the T wave of the preceding complex to such a degree that neither the P-R interval nor the Q-T interval is measurable. The intervals and pulse rate used were all taken when the pulse had slowed sufficiently to permit separa-

tion of the components of the complex. The data are summarized in Table 1. Ten children showed a shortened P-R interval, ten showed no change, and six showed a prolongation of the P-R interval. In no case was the change in excess of 0.02 second. Average changes in pulse rate were similar in all groups and the range of change in pulse rates in individuals who showed increased P-R duration and those who showed decreased duration was very similar. The only apparent difference is that those who showed increased P-R duration did so at a point somewhat later after exercise than those who showed shortened intervals. Within this group of healthy children it is apparent that acceleration of the pulse rate by exercise produced no uniform or predictable change in the duration of the P-R interval regardless of the amount of acceleration. Changes were individually oriented and in no case in excess of changes found in healthy children and young adults in the absence of pulse acceleration.

The statement that increased heart size from infancy to adult life is responsible for the increased length of the P-R interval that is associated with aging is frequently made in the literature (2, 9). This association is doubtful on several logical grounds, including the lack of similarity between established physical growth curves and the curve for the P-R interval, which shows no adolescent increase and essentially completes its increase by the age of 10 years. Also, the total increase in duration of the P-R interval is of the order of 25% of the infancy value, while cardiac size increases approximately four fold in transverse diameter and ten fold in weight. A com-

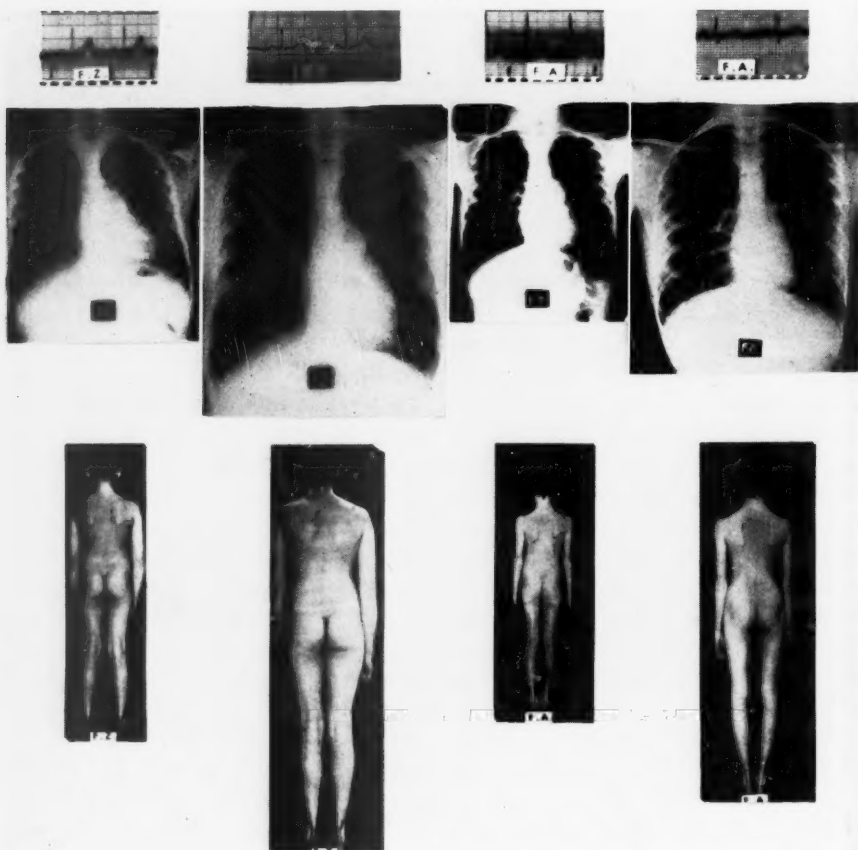
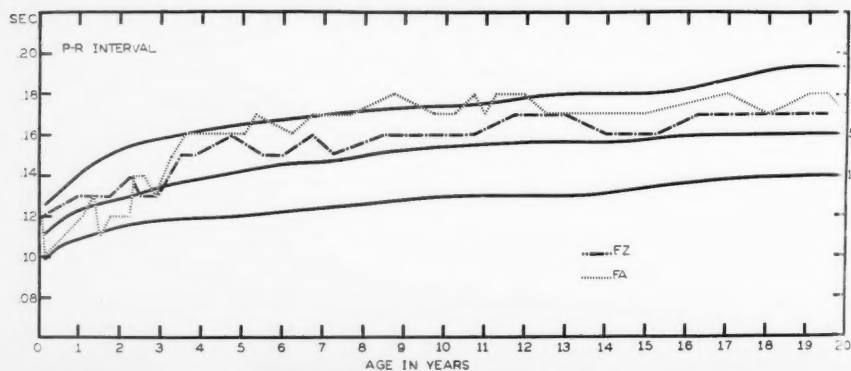


Fig. 7. P-R intervals, chest films, ECG tracings and posture photos of a boy and a girl to illustrate the lack of correlation between heart size or heart growth and the duration of the P-R interval.

Fig. 8.

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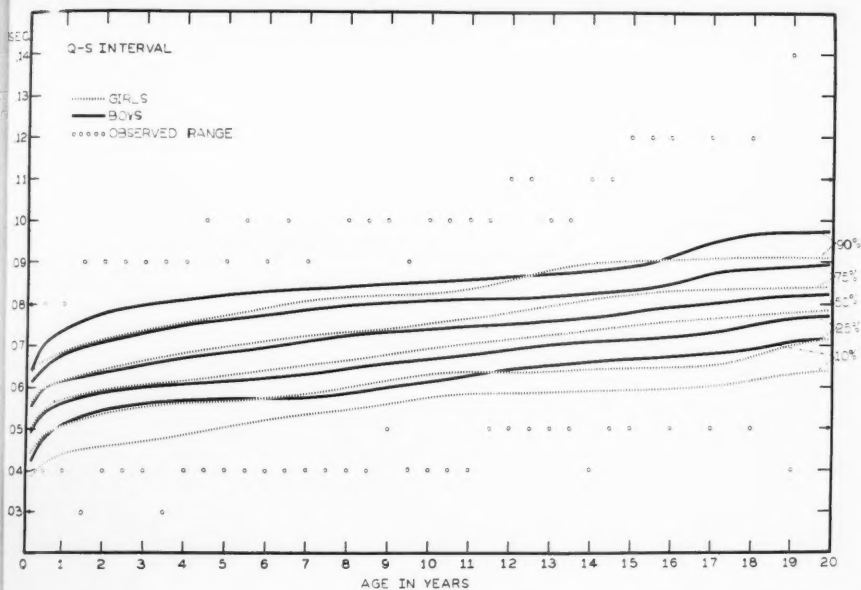


Fig. 8. Percentile standards and observed range of Q-S interval duration for healthy subjects from 2 months to 20 years.

parison of the duration of the P-R intervals with the size of the heart as measured on chest X-rays of children of this study showed no similarity between the two. A child or young adult with a very small heart or a very large heart may have a P-R interval at any point within the observed range. Fig. 7 illustrates the lack of correlation between heart size at any given age and the duration of the P-R interval. It also shows the absence of influence of growth changes on this interval. F. Z. and F. A. both have P-R intervals between the 50th percentile and 90th percentile lines, with F. A. having a slightly longer interval than F. Z. The girl was quite small, had a limited amount of adolescent growth and became a very small young woman. F. Z. was a large boy who had a very large adoles-

cent growth increase producing a very large young man. Heart size increases with weight (22) and as may be seen from the reproductions of the chest films, F. Z. had a much larger increase than F. A. without similar change in the relative or absolute duration of the P-R interval. It may be seen also that the P-R increase in both children was essentially complete at the time of the 8-year films, while body and heart size changed markedly between 8 years and 18 years.

The Q-S Interval

Fig. 8 illustrates the standards for the Q-S interval derived from the data. There are definite differences in the standards for boys and girls, and, at least in the 90th percentile line, there is what appears

TABLE 6. *Lead I. Percentile distribution of Q-S interval (boys).*

Age	10th %	25th %	50th %	75th %	90th %	No.	Age
0-1	0.0373	0.0418	0.0484	0.0543	0.0611	47	12-0
0-2	0.0427	0.0482	0.0550	0.0611	0.0647	47	12-3
0-3	0.0451	0.0519	0.0584	0.0631	0.0688	47	12-6
0-4	0.0400	0.0500	0.0579	0.0614	0.0636	23	12-9
0-5	0.0487	0.0542	0.0600	0.0662	0.0745	17	13-0
0-6	0.0465	0.0535	0.0588	0.0632	0.0683	6	13-3
0-9	0.0475	0.0535	0.0592	0.0642	0.0714	53	13-6
1-0	0.0502	0.0562	0.0603	0.0644	0.0729	57	13-9
1-3	0.0474	0.0558	0.0609	0.0669	0.0728	47	14-0
1-6	0.0470	0.0555	0.0607	0.0679	0.0777	48	14-6
1-9	0.0542	0.0577	0.0625	0.0689	0.0739	49	15-0
2-0	0.0522	0.0571	0.0615	0.0678	0.0758	49	15-6
2-3	0.0550	0.0581	0.0633	0.0703	0.0750	60	16-0
2-6	0.0525	0.0575	0.0626	0.0698	0.0758	57	17-0
2-9	0.0538	0.0581	0.0636	0.0707	0.0758	57	18-0
3-0	0.0558	0.0584	0.0629	0.0714	0.0792	53	19-0
3-3	0.0547	0.0586	0.0648	0.0723	0.0794	49	20-0
3-6	0.0538	0.0577	0.0627	0.0705	0.0777	44	21-0
3-9	0.0565	0.0593	0.0641	0.0710	0.0762	44	22-0
4-0	0.0560	0.0590	0.0640	0.0727	0.0804	42	23-0
4-3	0.0550	0.0578	0.0625	0.0694	0.0750	39	24-0
4-6	0.0560	0.0595	0.0656	0.0764	0.0822	37	
4-9	0.0517	0.0581	0.0644	0.0725	0.0793	49	
5-0	0.0566	0.0600	0.0659	0.0736	0.0801	34	
5-3	0.0560	0.0600	0.0665	0.0727	0.0795	32	
5-6	0.0551	0.0590	0.0655	0.0732	0.0798	30	
5-9	0.0580	0.0646	0.0704	0.0764	0.0816	31	Age
6-0	0.0556	0.0590	0.0646	0.0739	0.0805	27	
6-3	0.0559	0.0606	0.0688	0.0772	0.0819	28	0-1
6-6	0.0569	0.0597	0.0643	0.0750	0.0810	24	0-2
6-9	0.0530	0.0600	0.0693	0.0783	0.0843	24	0-3
7-0	0.0553	0.0592	0.0658	0.0723	0.0790	34	0-4
7-3	0.0563	0.0633	0.0710	0.0783	0.0830	28	0-5
7-6	0.0567	0.0602	0.0662	0.0733	0.0797	37	0-6
7-9	0.0552	0.0604	0.0692	0.0775	0.0820	21	0-9
8-0	0.0596	0.0658	0.0722	0.0786	0.0824	28	1-0
8-3	0.0562	0.0610	0.0686	0.0762	0.0822	32	1-3
8-6	0.0572	0.0606	0.0669	0.0754	0.0822	27	1-6
8-9	0.0594	0.0657	0.0736	0.0795	0.0828	28	1-9
9-0	0.0580	0.0625	0.0700	0.0775	0.0820	27	2-0
9-3	0.0568	0.0646	0.0700	0.0754	0.0832	31	2-3
9-6	0.0530	0.0600	0.0717	0.0794	0.0828	18	2-6
9-9	0.0566	0.0606	0.0675	0.0750	0.0822	24	2-9
10-0	0.0574	0.0611	0.0675	0.0746	0.0827	17	3-0
10-3	0.0590	0.0650	0.0712	0.0780	0.0828	32	3-3
10-6	0.0570	0.0621	0.0690	0.0750	0.0822	29	3-6
10-9	0.0610	0.0662	0.0700	0.0738	0.0790	12	3-9
11-0	0.0592	0.0654	0.0729	0.0804	0.0849	21	4-0
11-3	0.0579	0.0622	0.0761	0.0812	0.0844	29	4-3
11-6	0.0563	0.0604	0.0688	0.0782	0.0823	19	4-6
11-9	0.0562	0.0619	0.0692	0.0756	0.0812	15	4-9

Table 6, cont.

Age	10th %	25th %	50th %	75th %	90th %	No.
12-0	0.0585	0.0638	0.0725	0.0804	0.0849	21
12-3	0.0537	0.0692	0.0780	0.0845	0.0963	26
12-6	0.0578	0.0652	0.0700	0.0748	0.0822	21
12-9	0.0582	0.0629	0.0720	0.0791	0.0826	19
13-0	0.0588	0.0645	0.0700	0.0756	0.0828	19
13-3	0.0554	0.0620	0.0700	0.0775	0.0830	22
13-6	0.0517	0.0650	0.0733	0.0817	0.0883	20
13-9	0.0578	0.0620	0.0717	0.0800	0.0842	14
14-0	0.0653	0.0683	0.0733	0.0794	0.0834	24
14-6	0.0558	0.0644	0.0742	0.0808	0.0847	23
15-0	0.0582	0.0658	0.0715	0.0778	0.0821	23
15-6	0.0615	0.0689	0.0767	0.0831	0.0907	23
16-0	0.0612	0.0684	0.0767	0.0818	0.0849	31
17-0	0.0625	0.0698	0.0778	0.0834	0.0920	45
18-0	0.0650	0.0725	0.0788	0.0834	0.0975	30
19-0	0.0650	0.0761	0.0817	0.0883	0.0933	20
20-0	0.0687	0.0758	0.0793	0.0828	0.0849	21
21-0	0.0668	0.0725	0.0789	0.0842	0.0955	19
22-0	0.0668	0.0725	0.0808	0.0981	0.1055	19
23-0	0.0680	0.0767	0.0833	0.0925	0.1090	16
24-0	0.0630	0.0750	0.0817	0.1000	0.1120	16

TABLE 7. Lead I. Percentile distribution of Q-S interval (girls).

Age	10th %	25th %	50th %	75th %	90th %	No.
0-1	0.0372	0.0411	0.0484	0.0572	0.0635	63
0-2	0.0393	0.0454	0.0510	0.0581	0.0645	56
0-3	0.0392	0.0454	0.0528	0.0604	0.0653	59
0-4	0.0476	0.0545	0.0619	0.0696	0.0746	23
0-5	0.0435	0.0506	0.0586	0.0646	0.0708	17
0-6	0.0453	0.0499	0.0571	0.0637	0.0719	55
0-9	0.0459	0.0514	0.0585	0.0641	0.0708	52
1-0	0.0457	0.0508	0.0576	0.0627	0.0698	51
1-3	0.0444	0.0506	0.0577	0.0626	0.0693	47
1-6	0.0475	0.0535	0.0591	0.0639	0.0730	52
1-9	0.0437	0.0550	0.0598	0.0646	0.0747	52
2-0	0.0474	0.0530	0.0590	0.0641	0.0718	59
2-3	0.0480	0.0557	0.0611	0.0681	0.0750	60
2-6	0.0500	0.0571	0.0622	0.0698	0.0775	55
2-9	0.0506	0.0569	0.0616	0.0680	0.0744	59
3-0	0.0499	0.0564	0.0607	0.0652	0.0741	59
3-3	0.0473	0.0568	0.0611	0.0669	0.0782	47
3-6	0.0483	0.0550	0.0603	0.0664	0.0750	40
3-9	0.0482	0.0557	0.0612	0.0694	0.0784	46
4-0	0.0515	0.0587	0.0661	0.0721	0.0773	46
4-3	0.0481	0.0558	0.0613	0.0694	0.0780	42
4-6	0.0505	0.0562	0.0608	0.0659	0.0721	33
4-9	0.0492	0.0561	0.0609	0.0671	0.0748	31

Table 7, cont.

Age	10th %	25th %	50th %	75th %	90th %	No.	Age
5-0	0.0490	0.0560	0.0623	0.0700	0.0757	29	0-1
5-3	0.0556	0.0586	0.0636	0.0721	0.0794	29	0-2
5-6	0.0487	0.0559	0.0632	0.0725	0.0820	31	0-3
5-9	0.0538	0.0573	0.0614	0.0671	0.0762	31	0-4
6-0	0.0552	0.0583	0.0634	0.0722	0.0804	31	0-5
6-3	0.0490	0.0550	0.0620	0.0707	0.0780	29	0-6
6-6	0.0488	0.0561	0.0618	0.0719	0.0812	27	0-9
6-9	0.0505	0.0573	0.0635	0.0762	0.0822	31	1-0
7-0	0.0490	0.0562	0.0612	0.0680	0.0763	29	1-3
7-3	0.0522	0.0580	0.0645	0.0762	0.0835	29	1-6
7-6	0.0554	0.0586	0.0641	0.0733	0.0802	29	1-9
7-9	0.0557	0.0592	0.0650	0.0728	0.0823	29	2-0
8-0	0.0513	0.0569	0.0612	0.0669	0.0778	29	2-3
8-3	0.0556	0.0590	0.0646	0.0739	0.0816	27	2-6
8-6	0.0520	0.0653	0.0700	0.0747	0.0808	17	2-9
8-9	0.0554	0.0585	0.0638	0.0762	0.0825	27	3-0
9-0	0.0557	0.0595	0.0662	0.0750	0.0810	29	3-3
9-3	0.0500	0.0578	0.0657	0.0746	0.0820	27	3-6
9-6	0.0571	0.0604	0.0658	0.0721	0.0775	15	3-9
9-9	0.0566	0.0620	0.0693	0.0760	0.0814	19	4-0
10-0	0.0495	0.0572	0.0631	0.0755	0.0812	19	4-3
10-3	0.0540	0.0590	0.0667	0.0779	0.0839	19	4-6
10-6	0.0575	0.0612	0.0680	0.0756	0.0812	15	4-9
10-9	0.0558	0.0596	0.0658	0.0721	0.0775	15	5-0
11-0	0.0557	0.0589	0.0643	0.0758	0.0833	15	5-3
11-3	0.0530	0.0600	0.0725	0.0806	0.0846	24	5-6
11-6	0.0580	0.0625	0.0700	0.0775	0.0820	15	5-9
11-9	0.0592	0.0653	0.0706	0.0765	0.0816	17	6-0
12-0	0.0556	0.0584	0.0631	0.0758	0.0833	15	6-3
12-3	0.0558	0.0588	0.0638	0.0810	0.0890	16	6-6
12-6	0.0633	0.0673	0.0718	0.0779	0.0842	25	6-9
12-9	0.0580	0.0625	0.0700	0.0775	0.0820	9	7-0
13-0	0.0570	0.0630	0.0717	0.0788	0.0825	26	7-3
13-3	0.0582	0.0631	0.0712	0.0794	0.0842	15	7-6
13-6	0.0566	0.0620	0.0700	0.0788	0.0860	19	7-9
13-9	0.0600	0.0662	0.0725	0.0788	0.0825	15	8-0
14-0	0.0580	0.0661	0.0729	0.0791	0.0826	19	8-3
14-6	0.0520	0.0625	0.0700	0.0767	0.0837	14	8-6
15-0	0.0571	0.0618	0.0706	0.0789	0.0831	31	8-9
15-3	0.0583	0.0633	0.0690	0.0740	0.0800	16	9-0
16-0	0.0561	0.0611	0.0717	0.0800	0.0841	30	9-3
17-0	0.0570	0.0614	0.0717	0.0805	0.0848	31	9-6
18-0	0.0587	0.0642	0.0750	0.0819	0.0890	22	9-9
19-0	0.0572	0.0635	0.0700	0.0769	0.0848	21	10-0
20-0	0.0582	0.0629	0.0738	0.0821	0.0955	19	10-3
21-0	0.0573	0.0656	0.0756	0.0809	0.0841	17	10-6
22-0	0.0540	0.0592	0.0767	0.0842	0.0905	9	10-9
23-0	0.0515	0.0656	0.0738	0.0819	0.0920	13	11-0
24-0	0.0550	0.0625	0.0783	0.0867	0.0917	16	11-3
							11-6
							11-9

TABLE 8. *Lead II. Percentile distribution of Q-S interval (boys).*

No.	Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
24	0-1	0.03	0.0391	0.0451	0.0511	0.0581	0.0638	0.08	45
24	0-2	0.03	0.0440	0.0498	0.0570	0.0618	0.0648	0.07	45
32	0-3	0.04	0.0432	0.0516	0.0579	0.0618	0.0642	0.08	41
32	0-4	0.04	0.0470	0.0530	0.0586	0.0632	0.0700	0.08	20
33	0-5	0.05	0.0551	0.0572	0.0606	0.0641	0.0695	0.08	11
24	0-6	0.04	0.0492	0.0557	0.0609	0.0671	0.0736	0.08	60
24	0-9	0.04	0.0486	0.0558	0.0608	0.0670	0.0748	0.08	52
32	1-0	0.04	0.0507	0.0564	0.0612	0.0673	0.0744	0.08	57
24	1-3	0.04	0.0542	0.0575	0.0619	0.0675	0.0729	0.08	47
24	1-6	0.04	0.0518	0.0572	0.0620	0.0690	0.0762	0.08	44
24	1-9	0.04	0.0544	0.0574	0.0616	0.0678	0.0772	0.08	47
24	2-0	0.04	0.0561	0.0590	0.0638	0.0710	0.0770	0.08	48
24	2-3	0.04	0.0525	0.0577	0.0635	0.0723	0.0795	0.08	60
24	2-6	0.04	0.0556	0.0590	0.0646	0.0718	0.0780	0.08	56
17	2-9	0.04	0.0556	0.0589	0.0644	0.0722	0.0789	0.08	55
24	3-0	0.04	0.0559	0.0592	0.0646	0.0736	0.0808	0.09	52
24	3-3	0.04	0.0566	0.0607	0.0671	0.0730	0.0789	0.09	49
24	3-6	0.05	0.0563	0.0600	0.0665	0.0750	0.0810	0.09	44
17	3-9	0.04	0.0573	0.0608	0.0668	0.0732	0.0795	0.08	44
18	4-0	0.04	0.0552	0.0604	0.0683	0.0755	0.0818	0.09	42
19	4-3	0.04	0.0558	0.0591	0.0646	0.0710	0.0749	0.08	31
24	4-6	0.05	0.0569	0.0607	0.0677	0.0761	0.0821	0.09	36
15	4-9	0.04	0.0575	0.0612	0.0686	0.0773	0.0819	0.08	40
17	5-0	0.04	0.0553	0.0589	0.0650	0.0735	0.0810	0.09	34
15	5-3	0.04	0.0552	0.0595	0.0679	0.0777	0.0821	0.09	32
24	5-6	0.04	0.0561	0.0608	0.0679	0.0744	0.0815	0.09	31
15	5-9	0.04	0.0602	0.0662	0.0713	0.0772	0.0819	0.08	31
17	6-0	0.04	0.0540	0.0590	0.0667	0.0775	0.0828	0.09	28
15	6-3	0.04	0.0590	0.0650	0.0720	0.0790	0.0832	0.09	28
16	6-6	0.04	0.0558	0.0600	0.0672	0.0750	0.0820	0.09	28
24	6-9	0.05	0.0584	0.0636	0.0721	0.0800	0.0845	0.09	24
9	7-0	0.05	0.0577	0.0633	0.0697	0.0756	0.0812	0.09	34
20	7-3	0.05	0.0590	0.0650	0.0738	0.0817	0.0880	0.09	28
13	7-6	0.04	0.0556	0.0607	0.0691	0.0773	0.0819	0.08	37
18	7-9	0.04	0.0580	0.0625	0.0764	0.0811	0.0840	0.09	21
15	8-0	0.06	0.0596	0.0657	0.0709	0.0768	0.0817	0.08	23
19	8-3	0.04	0.0603	0.0683	0.0772	0.0817	0.0843	0.10	32
14	8-6	0.06	0.0590	0.0650	0.0728	0.0795	0.0834	0.09	28
31	8-9	0.06	0.0578	0.0619	0.0700	0.0781	0.0822	0.09	22
10	9-0	0.06	0.0589	0.0646	0.0743	0.0807	0.0844	0.10	27
30	9-3	0.05	0.0602	0.0663	0.0723	0.0821	0.0898	0.09	31
32	9-6	0.04	0.0610	0.0680	0.0760	0.0805	0.0832	0.08	18
24	9-9	0.05	0.0598	0.0661	0.0728	0.0794	0.0834	0.09	24
21	10-0	0.06	0.0582	0.0630	0.0725	0.0800	0.0840	0.10	16
19	10-3	0.05	0.0630	0.0681	0.0742	0.0804	0.0841	0.09	32
17	10-6	0.04	0.0598	0.0664	0.0750	0.0805	0.0837	0.10	24
9	10-9	0.06	0.0653	0.0683	0.0733	0.0817	0.0890	0.09	12
13	11-0	0.04	0.0651	0.0686	0.0744	0.0809	0.0849	0.09	21
10	11-3	0.05	0.0608	0.0666	0.0718	0.0784	0.0839	0.12	29
	11-6	0.05	0.0661	0.0697	0.0756	0.0816	0.0855	0.09	19
	11-9	0.05	0.0625	0.0669	0.0711	0.0756	0.0812	0.09	15

Table 8, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	N	Age
12-0	0.05	0.0668	0.0721	0.0782	0.0830	0.0880	0.10	2	5-0
12-3	0.05	0.0630	0.0700	0.0783	0.0862	0.0963	0.10	2	5-3
12-6	0.05	0.0651	0.0696	0.0767	0.0825	0.0880	0.09	2	5-6
12-9	0.06	0.0663	0.0704	0.0764	0.0807	0.0833	0.10	1	5-9
13-0	0.05	0.0660	0.0692	0.0744	0.0803	0.0839	0.10	1	6-0
13-3	0.05	0.0580	0.0658	0.0750	0.0805	0.0838	0.10	2	6-3
13-6	0.05	0.0675	0.0712	0.0772	0.0828	0.0900	0.10	2	6-6
13-9	0.05	0.0620	0.0675	0.0733	0.0800	0.0842	0.09	1	6-9
14-0	0.04	0.0666	0.0706	0.0764	0.0807	0.0833	0.11	2	7-0
14-6	0.05	0.0658	0.0744	0.0796	0.0844	0.0940	0.11	2	7-3
15-0	0.05	0.0654	0.0704	0.0775	0.0832	0.0892	0.10	2	7-6
15-6	0.05	0.0665	0.0762	0.0804	0.0845	0.0985	0.11	2	7-9
16-0	0.05	0.0662	0.0710	0.0777	0.0830	0.0886	0.12	2	8-0
17-0	0.06	0.0656	0.0725	0.0806	0.0895	0.0978	0.12	4	8-3
18-0	0.06	0.0708	0.0764	0.0809	0.0869	0.0978	0.11	2	8-6
19-0	0.05	0.0690	0.0750	0.0812	0.0900	0.0983	0.14	2	8-9
20-0	0.05	0.0758	0.0783	0.0823	0.0879	0.0932	0.10	2	9-0
21-0	0.05	0.0695	0.0775	0.0843	0.0935	0.1002	0.12	1	9-3
22-0	0.06	0.0763	0.0804	0.0875	0.0962	0.1105	0.13	1	9-6
23-0	0.05	0.0665	0.0725	0.0850	0.0950	0.1090	0.12	1	9-9
24-0	0.06	0.0630	0.0717	0.0910	0.0990	0.1038	0.12	1	10-0

TABLE 9. *Lead II. Percentile distribution of Q-S interval (girls).*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	N	Age
0-1	0.03	0.0377	0.0418	0.0484	0.0547	0.0612	0.08	6	12-0
0-2	0.03	0.0388	0.0453	0.0508	0.0573	0.0632	0.08	5	12-3
0-3	0.03	0.0384	0.0446	0.0500	0.0555	0.0634	0.08	5	12-6
0-4	0.04	0.0154	0.0504	0.0575	0.0632	0.0707	0.08	2	12-9
0-5	0.04	0.0435	0.0482	0.0543	0.0604	0.0640	0.07	1	13-0
0-6	0.04	0.0411	0.0476	0.0552	0.0612	0.0648	0.08	5	13-3
0-9	0.04	0.0415	0.0481	0.0560	0.0625	0.0690	0.08	5	13-6
1-0	0.04	0.0461	0.0500	0.0562	0.0614	0.0645	0.08	5	13-9
1-3	0.04	0.0428	0.0488	0.0562	0.0618	0.0660	0.09	4	14-0
1-6	0.03	0.0450	0.0512	0.0580	0.0626	0.0670	0.09	5	14-6
1-9	0.04	0.0456	0.0499	0.0563	0.0612	0.0642	0.09	5	15-0
2-0	0.04	0.0464	0.0527	0.0593	0.0647	0.0740	0.09	5	16-0
2-3	0.04	0.0464	0.0560	0.0610	0.0673	0.0742	0.08	6	17-0
2-6	0.04	0.0458	0.0559	0.0607	0.0666	0.0780	0.09	5	18-0
2-9	0.04	0.0469	0.0553	0.0603	0.0661	0.0742	0.09	5	19-0
3-0	0.04	0.0450	0.0525	0.0591	0.0643	0.0738	0.09	6	20-0
3-3	0.04	0.0530	0.0572	0.0617	0.0677	0.0743	0.09	4	21-0
3-6	0.03	0.0464	0.0550	0.0603	0.0667	0.0770	0.08	4	22-0
3-9	0.04	0.0425	0.0560	0.0611	0.0678	0.0745	0.09	4	23-0
4-0	0.04	0.0493	0.0572	0.0644	0.0708	0.0747	0.08	4	24-0
4-3	0.04	0.0490	0.0558	0.0613	0.0685	0.0748	0.09	4	
4-6	0.04	0.0507	0.0569	0.0618	0.0678	0.0727	0.10	3	
4-9	0.04	0.0487	0.0557	0.0610	0.0675	0.0735	0.09	3	

Table . cont.

No.	Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
	5-0	0.04	0.0526	0.0575	0.0628	0.0711	0.0794	0.09	38
	5-3	0.04	0.0530	0.0583	0.0642	0.0725	0.0805	0.09	28
	5-6	0.04	0.0494	0.0563	0.0617	0.0710	0.0806	0.10	32
	5-9	0.04	0.0486	0.0554	0.0603	0.0654	0.0729	0.08	35
	6-0	0.04	0.0527	0.0578	0.0633	0.0708	0.0768	0.09	33
	6-3	0.04	0.0495	0.0564	0.0614	0.0683	0.0757	0.08	28
	6-6	0.04	0.0533	0.0591	0.0675	0.0775	0.0829	0.10	25
	6-9	0.04	0.0530	0.0581	0.0642	0.0720	0.0810	0.09	32
	7-0	0.04	0.0515	0.0568	0.0614	0.0680	0.0763	0.08	26
	7-3	0.04	0.0513	0.0591	0.0681	0.0779	0.0855	0.12	29
	7-6	0.04	0.0564	0.0600	0.0664	0.0750	0.0810	0.08	24
	7-9	0.05	0.0520	0.0577	0.0641	0.0717	0.0810	0.10	28
	8-0	0.04	0.0558	0.0594	0.0654	0.0715	0.0755	0.10	29
	8-3	0.05	0.0584	0.0656	0.0712	0.0778	0.0829	0.10	27
	8-6	0.04	0.0559	0.0591	0.0644	0.0725	0.0815	0.10	17
	8-9	0.04	0.0533	0.0604	0.0694	0.0775	0.0829	0.10	25
	9-0	0.05	0.0560	0.0608	0.0682	0.0748	0.0818	0.10	29
	9-3	0.04	0.0557	0.0611	0.0685	0.0748	0.0820	0.11	25
	9-6	0.04	0.0569	0.0597	0.0644	0.0715	0.0775	0.09	15
	9-9	0.05	0.0563	0.0608	0.0679	0.0743	0.0805	0.09	18
	10-0	0.04	0.0588	0.0645	0.0691	0.0734	0.0787	0.08	19
	10-3	0.04	0.0567	0.0608	0.0692	0.0791	0.0841	0.12	27
	10-6	0.06	0.0656	0.0686	0.0736	0.0800	0.0842	0.10	14
	10-9	0.04	0.0562	0.0619	0.0692	0.0756	0.0812	0.08	15
	11-0	0.05	0.0569	0.0597	0.0644	0.0731	0.0800	0.10	15
	11-3	0.05	0.0570	0.0621	0.0750	0.0817	0.0980	0.12	24
	11-6	0.05	0.0525	0.0594	0.0680	0.0758	0.0833	0.10	15
	11-9	0.04	0.0520	0.0554	0.0714	0.0779	0.0822	0.08	17
	12-0	0.05	0.0569	0.0597	0.0644	0.0781	0.0838	0.11	15
	12-3	0.05	0.0573	0.0607	0.0683	0.0790	0.0838	0.10	16
	12-6	0.06	0.0600	0.0660	0.0712	0.0794	0.0900	0.11	25
	12-9	0.06	0.0580	0.0625	0.0700	0.0788	0.0960	0.11	9
	13-0	0.05	0.0567	0.0617	0.0700	0.0779	0.0821	0.08	20
	13-3	0.05	0.0593	0.0654	0.0708	0.0775	0.0840	0.10	13
	13-6	0.05	0.0610	0.0675	0.0750	0.0814	0.0870	0.09	18
	13-9	0.06	0.0600	0.0665	0.0740	0.0804	0.0842	0.11	15
	14-0	0.04	0.0568	0.0625	0.0755	0.0802	0.0831	0.09	19
	14-6	0.05	0.0620	0.0680	0.0750	0.0820	0.0980	0.11	14
	15-0	0.05	0.0569	0.0611	0.0708	0.0816	0.0945	0.12	31
	16-0	0.05	0.0577	0.0618	0.0700	0.0789	0.0839	0.12	30
	17-0	0.05	0.0594	0.0679	0.0771	0.0829	0.0895	0.10	32
	18-0	0.05	0.0623	0.0692	0.0775	0.0844	0.0995	0.12	22
	19-0	0.04	0.0578	0.0655	0.0755	0.0808	0.0839	0.12	21
	20-0	0.05	0.0675	0.0750	0.0788	0.0827	0.0900	0.11	20
	21-0	0.05	0.0585	0.0712	0.0789	0.0836	0.0915	0.11	17
	22-0	0.05	0.0740	0.0768	0.0800	0.0832	0.0860	0.11	9
	23-0	0.05	0.0615	0.0753	0.0789	0.0825	0.0847	0.11	13
	24-0	0.05	0.0600	0.0762	0.0825	0.0900	0.1050	0.12	10

TABLE 10. *Lead III. Percentile distribution of Q-S interval (boys).*

Age	10th %	25th %	50th %	75th %	90th %	Age
0-1	0.0387	0.0442	0.0521	0.0594	0.0635	12-0
0-2	0.0410	0.0488	0.0568	0.0620	0.0658	12-3
0-3	0.0451	0.0507	0.0576	0.0625	0.0668	12-6
0-4	0.0450	0.0510	0.0580	0.0630	0.0700	12-9
0-5	0.0505	0.0562	0.0608	0.0675	0.0795	13-0
0-6	0.0478	0.0554	0.0596	0.0637	0.0753	13-3
0-9	0.0488	0.0553	0.0598	0.0643	0.0747	13-6
1-0	0.0499	0.0567	0.0617	0.0682	0.0740	13-9
1-3	0.0501	0.0565	0.0612	0.0675	0.0744	14-0
1-6	0.0476	0.0563	0.0614	0.0686	0.0764	14-6
1-9	0.0495	0.0560	0.0606	0.0658	0.0773	15-0
2-0	0.0508	0.0574	0.0636	0.0723	0.0794	15-6
2-3	0.0500	0.0565	0.0623	0.0703	0.0775	16-0
2-6	0.0533	0.0579	0.0630	0.0705	0.0771	17-0
2-9	0.0525	0.0578	0.0635	0.0714	0.0781	18-0
3-0	0.0512	0.0574	0.0627	0.0706	0.0782	19-0
3-3	0.0545	0.0590	0.0659	0.0736	0.0807	20-0
3-6	0.0536	0.0577	0.0629	0.0702	0.0768	21-0
3-9	0.0560	0.0588	0.0633	0.0704	0.0762	22-0
4-0	0.0561	0.0593	0.0647	0.0739	0.0811	23-0
4-3	0.0500	0.0575	0.0650	0.0725	0.0790	24-0
4-6	0.0560	0.0594	0.0650	0.0761	0.0821	
4-9	0.0566	0.0615	0.0689	0.0761	0.0815	
5-0	0.0559	0.0593	0.0650	0.0735	0.0810	
5-3	0.0552	0.0595	0.0683	0.0794	0.0848	
5-6	0.0568	0.0606	0.0678	0.0766	0.0824	
5-9	0.0551	0.0593	0.0667	0.0753	0.0811	Age
6-0	0.0557	0.0595	0.0662	0.0750	0.0810	
6-3	0.0576	0.0636	0.0705	0.0772	0.0819	0-1
6-6	0.0564	0.0596	0.0650	0.0750	0.0820	0-2
6-9	0.0572	0.0629	0.0706	0.0782	0.0831	0-3
7-0	0.0567	0.0604	0.0679	0.0779	0.0822	0-4
7-3	0.0585	0.0638	0.0750	0.0814	0.0857	0-5
7-6	0.0572	0.0619	0.0705	0.0784	0.0824	0-6
7-9	0.0505	0.0625	0.0740	0.0809	0.0849	0-9
8-0	0.0565	0.0668	0.0725	0.0786	0.0824	1-0
8-3	0.0605	0.0692	0.0769	0.0829	0.0898	1-3
8-6	0.0584	0.0634	0.0729	0.0798	0.0835	1-6
8-9	0.0575	0.0612	0.0750	0.0812	0.0850	1-9
9-0	0.0589	0.0646	0.0731	0.0802	0.0843	2-0
9-3	0.0589	0.0647	0.0744	0.0810	0.0849	2-3
9-6	0.0630	0.0712	0.0775	0.0812	0.0835	2-6
9-9	0.0558	0.0630	0.0706	0.0790	0.0870	2-9
10-0	0.0578	0.0621	0.0700	0.0808	0.0893	3-0
10-3	0.0623	0.0683	0.0750	0.0812	0.0848	3-3
10-6	0.0610	0.0675	0.0750	0.0810	0.0846	3-6
10-9	0.0654	0.0690	0.0750	0.0810	0.0846	3-9
11-0	0.0572	0.0635	0.0767	0.0825	0.0880	4-0
11-3	0.0588	0.0666	0.0754	0.0815	0.0855	4-3
11-6	0.0572	0.0644	0.0740	0.0811	0.0855	4-6
11-9	0.0525	0.0688	0.0778	0.0819	0.0844	4-9

Table 10, cont.

Age	10th %	25th %	50th %	75th %	90th %	No.
12-0	0.0605	0.0682	0.0757	0.0832	0.0913	21
12-3	0.0603	0.0686	0.0779	0.0880	0.0963	26
12-6	0.0651	0.0696	0.0765	0.0818	0.0849	21
12-9	0.0586	0.0640	0.0750	0.0825	0.0910	18
13-0	0.0545	0.0642	0.0740	0.0811	0.0955	19
13-3	0.0520	0.0595	0.0700	0.0805	0.0895	21
13-6	0.0650	0.0688	0.0750	0.0821	0.0900	20
13-9	0.0590	0.0700	0.0779	0.0829	0.0880	14
14-0	0.0578	0.0650	0.0736	0.0821	0.0930	24
14-6	0.0696	0.0756	0.0800	0.0844	0.0940	23
15-0	0.0576	0.0645	0.0729	0.0821	0.0935	23
15-6	0.0654	0.0704	0.0786	0.0892	0.1035	23
16-0	0.0652	0.0706	0.0781	0.0842	0.0945	32
17-0	0.0671	0.0757	0.0819	0.0914	0.1020	45
18-0	0.0677	0.0764	0.0814	0.0890	0.0990	28
19-0	0.0600	0.0750	0.0806	0.0883	0.1000	20
20-0	0.0700	0.0777	0.0823	0.0890	0.0950	20
21-0	0.0695	0.0794	0.0900	0.0995	0.1060	19
22-0	0.0759	0.0788	0.0835	0.0992	0.1160	19
23-0	0.0570	0.0675	0.0790	0.0975	0.1110	14
24-0	0.0603	0.0775	0.0950	0.1050	0.1170	16

TABLE 11. Lead III. Percentile distribution of Q-S interval (girls).

Age	10th %	25th %	50th %	75th %	90th %	No.
0-1	0.0394	0.0457	0.0531	0.0594	0.0630	62
0-2	0.0409	0.0468	0.0526	0.0598	0.0648	53
0-3	0.0403	0.0466	0.0518	0.0584	0.0639	58
0-4	0.0454	0.0504	0.0573	0.0625	0.0673	23
0-5	0.0378	0.0420	0.0550	0.0620	0.0680	14
0-6	0.0414	0.0480	0.0552	0.0621	0.0712	55
0-9	0.0437	0.0497	0.0571	0.0625	0.0680	52
1-0	0.0461	0.0500	0.0562	0.0617	0.0649	52
1-3	0.0428	0.0498	0.0572	0.0619	0.0647	47
1-6	0.0435	0.0506	0.0586	0.0646	0.0749	51
1-9	0.0476	0.0540	0.0593	0.0640	0.0765	51
2-0	0.0475	0.0551	0.0602	0.0658	0.0756	57
2-3	0.0459	0.0541	0.0602	0.0668	0.0750	60
2-6	0.0475	0.0563	0.0612	0.0675	0.0738	55
2-9	0.0482	0.0560	0.0615	0.0681	0.0733	59
3-0	0.0477	0.0560	0.0599	0.0638	0.0718	59
3-3	0.0484	0.0559	0.0621	0.0698	0.0758	47
3-6	0.0465	0.0554	0.0605	0.0666	0.0739	39
3-9	0.0475	0.0563	0.0629	0.0728	0.0806	45
4-0	0.0501	0.0565	0.0612	0.0673	0.0735	46
4-3	0.0485	0.0564	0.0628	0.0711	0.0782	41
4-6	0.0493	0.0572	0.0627	0.0703	0.0773	33
4-9	0.0476	0.0534	0.0615	0.0721	0.0798	31

Table 11, cont.

Age	10th %	25th %	50th %	75th %	90th %
5-0	0.0555	0.0592	0.0654	0.0725	0.0788
5-3	0.0510	0.0593	0.0680	0.0750	0.0810
5-6	0.0552	0.0592	0.0662	0.0764	0.0833
5-9	0.0478	0.0536	0.0608	0.0715	0.0800
6-0	0.0561	0.0605	0.0675	0.0742	0.0813
6-3	0.0535	0.0584	0.0645	0.0739	0.0805
6-6	0.0556	0.0603	0.0686	0.0775	0.0829
6-9	0.0510	0.0581	0.0642	0.0767	0.0847
7-0	0.0567	0.0608	0.0668	0.0712	0.0739
7-3	0.0498	0.0588	0.0708	0.0803	0.0860
7-6	0.0578	0.0650	0.0717	0.0783	0.0823
7-9	0.0558	0.0603	0.0678	0.0755	0.0836
8-0	0.0513	0.0596	0.0677	0.0733	0.0802
8-3	0.0571	0.0622	0.0740	0.0802	0.0836
8-6	0.0584	0.0635	0.0694	0.0747	0.0827
8-9	0.0533	0.0596	0.0678	0.0747	0.0820
9-0	0.0570	0.0658	0.0717	0.0788	0.0840
9-3	0.0500	0.0615	0.0695	0.0762	0.0825
9-6	0.0560	0.0605	0.0700	0.0806	0.0875
9-9	0.0586	0.0640	0.0717	0.0792	0.0837
10-0	0.0572	0.0644	0.0714	0.0782	0.0823
10-3	0.0584	0.0658	0.0733	0.0838	0.0916
10-6	0.0600	0.0661	0.0714	0.0781	0.0838
10-9	0.0500	0.0638	0.0738	0.0796	0.0829
11-0	0.0562	0.0619	0.0692	0.0758	0.0833
11-3	0.0610	0.0675	0.0750	0.0825	0.0930
11-6	0.0625	0.0694	0.0767	0.0808	0.0833
11-9	0.0584	0.0635	0.0700	0.0765	0.0816
12-0	0.0562	0.0619	0.0692	0.0762	0.0900
12-3	0.0577	0.0617	0.0717	0.0800	0.0840
12-6	0.0630	0.0710	0.0783	0.0833	0.0903
12-9	0.0595	0.0658	0.0733	0.0808	0.1060
13-0	0.0565	0.0612	0.0686	0.0755	0.0812
13-3	0.0565	0.0658	0.0760	0.0825	0.0985
13-6	0.0666	0.0720	0.0777	0.0818	0.0843
13-9	0.0625	0.0675	0.0729	0.0795	0.0840
14-0	0.0568	0.0625	0.0720	0.0796	0.0837
14-6	0.0585	0.0638	0.0750	0.0820	0.0910
15-0	0.0585	0.0657	0.0727	0.0825	0.1013
15-3	0.0700	0.0780	0.0830	0.0967	0.1017
16-0	0.0585	0.0638	0.0743	0.0806	0.0842
17-0	0.0603	0.0679	0.0769	0.0819	0.0849
18-0	0.0610	0.0733	0.0795	0.0845	0.1020
19-0	0.0605	0.0672	0.0725	0.0789	0.0834
20-0	0.0583	0.0675	0.0772	0.0828	0.0900
21-0	0.0585	0.0754	0.0814	0.0894	0.0980
22-0	0.0695	0.0756	0.0812	0.0888	0.1060
23-0	0.0680	0.0766	0.0806	0.0847	0.1020
24-0	0.0700	0.0775	0.0817	0.0875	0.1050

to be an adolescent spurt in the increments represented by the curve. The configuration of this percentile line is very like the curves for physical growth, with the earlier adolescence in the girls resulting in their curve crossing the curve for the boys until the later adolescent increase in the boys catches up and again exceeds the values for the girls. A tendency toward the same configuration is seen in the other percentile curves, with less and less prominence as the 10th percentile is approached. The total observed range illustrated is not divided by sex, the measurements used representing the longest and shortest intervals for any age in either sex. In this measurement there is very little increase in the range between the 10th and 90th percentiles from 2 months to 20 years (23) for either the boys or the girls, and the central 80 % of the range again agrees well with previously recorded standards. However, there is rather marked skewing of the data upward above the 90th percentile, which makes it very difficult to pick any level above which abnormality is presumed to be present (3, 24).

Examination of the curves of the Q-S measurement for individual children is less rewarding than it was for the P-R interval. With the very narrow total range for the group, a change of 0.01 second produces fluctuation through nearly half of the range between the 10th and 90th percentiles. Because of the frequency of coining of the terminal part of the QRS complex, the end of this interval is difficult to select in many instances, and variation between two observers of 0.01 second in this measurement is more common than in either the P-R interval or the Q-T interval. It is not surprising, therefore,

that curves for individuals show considerable fluctuation from age to age. The two individuals illustrated in Fig. 9 are both boys, selected to demonstrate that some adolescents do have an increase at the time of their physical adolescent growth spurts, while others fail to show such a change in spite of equally impressive physical changes. As may be seen from the photographs and the chest X-rays, these boys vary only a little from each other in general body size, though their Q-S measurements are quite widely separated within the group. It is true that those children whose Q-S durations fall nearer the 90th percentile more frequently show what appears to be an increase in the Q-S interval at the time of physical adolescence than do those whose Q-S intervals are near the 10th percentile, just as in the group data. It is also true that this pattern is not limited to them nor is it uniformly present in them. Finally, while the two boys illustrated stay fairly well within a single part of the group range, this is by no means always the case, and both temporary and long-term changes in level within the group are frequently observed.

The Q-T Interval

Investigators have varied markedly in their assessments of the clinical value of measurements of the Q-T interval between regarding it as a valuable prognostic sign in rheumatic disease (25, 27) through the middle ground of feeling that a better understanding of the things that cause it to vary in duration would improve its clinical usefulness (28), to the belief that it is of little if any clinical value (29). Since it represents electrical manifestations of

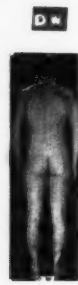
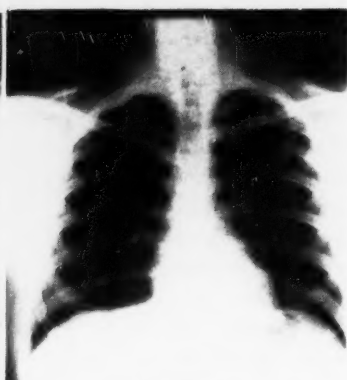
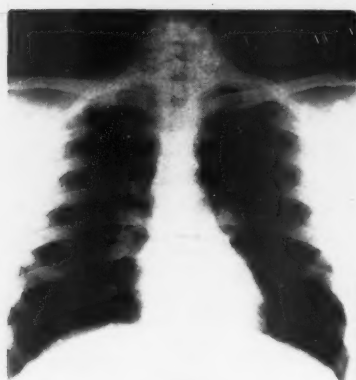
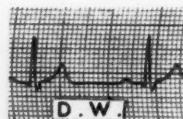
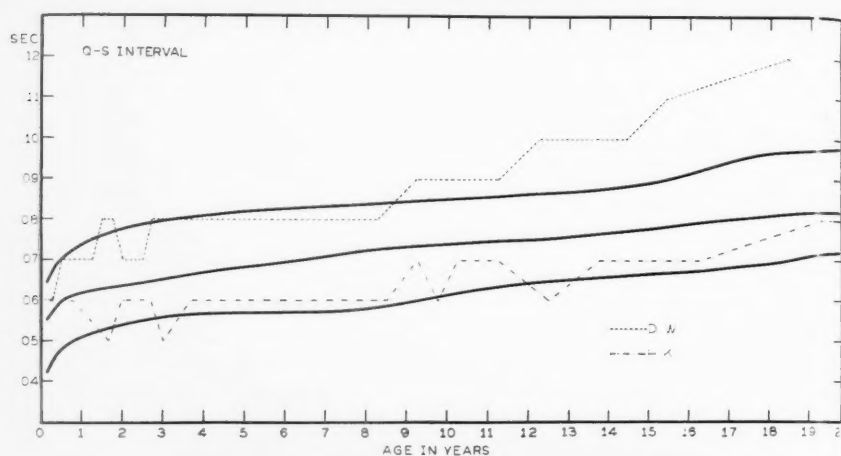


Fig. 9. Chest films, posture photos and graphic representation of the duration and development of the Q-S interval in two healthy boys, illustrating a pattern which parallels physical growth and one which does not. Lack of linear correspondence with heart size is also apparent

TABLE 12. *Lead I. Percentile distribution of Q-T interval.*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
0-1	0.19	0.2175	0.2282	0.2433	0.2604	0.2789	0.32	105
0-2	0.20	0.2290	0.2398	0.2542	0.2648	0.2838	0.32	98
0-3	0.20	0.2268	0.2421	0.2575	0.2748	0.2887	0.34	97
0-4	0.20	0.2330	0.2442	0.2636	0.2806	0.2957	0.36	42
0-5	0.24	0.2408	0.2553	0.2644	0.2792	0.2840	0.31	28
0-6	0.21	0.2374	0.2466	0.2587	0.2705	0.2843	0.32	114
0-9	0.20	0.2368	0.2438	0.2583	0.2681	0.2847	0.32	103
1-0	0.20	0.2359	0.2490	0.2617	0.2762	0.2843	0.30	109
1-3	0.21	0.2255	0.2488	0.2669	0.2826	0.2982	0.32	92
1-6	0.20	0.2421	0.2585	0.2766	0.2931	0.3154	0.36	94
1-9	0.22	0.2422	0.2595	0.2763	0.2880	0.3044	0.34	97
2-0	0.22	0.2571	0.2686	0.2810	0.2997	0.3194	0.36	105
2-3	0.23	0.2603	0.2761	0.2861	0.3028	0.3210	0.36	116
2-6	0.24	0.2615	0.2778	0.2891	0.3036	0.3204	0.36	110
2-9	0.24	0.2676	0.2795	0.2959	0.3114	0.3226	0.36	114
3-0	0.25	0.2667	0.2816	0.2979	0.3128	0.3240	0.37	111
3-3	0.24	0.2766	0.2856	0.3030	0.3161	0.3248	0.36	96
3-6	0.24	0.2776	0.2844	0.3027	0.3194	0.3340	0.38	84
3-9	0.26	0.2786	0.2867	0.3042	0.3197	0.3294	0.36	89
4-0	0.27	0.2826	0.2967	0.3083	0.3232	0.3410	0.38	88
4-3	0.26	0.2797	0.2906	0.3020	0.3200	0.3343	0.38	73
4-6	0.25	0.2846	0.2988	0.3166	0.3242	0.3510	0.40	68
4-9	0.26	0.2861	0.2992	0.3177	0.3243	0.3402	0.37	72
5-0	0.27	0.2957	0.3021	0.3177	0.3317	0.3500	0.40	72
5-3	0.26	0.2883	0.3062	0.3219	0.3375	0.3570	0.40	60
5-6	0.27	0.2887	0.3061	0.3200	0.3382	0.3547	0.38	64
5-9	0.28	0.2980	0.3125	0.3229	0.3389	0.3558	0.40	66
6-0	0.28	0.2918	0.3085	0.3213	0.3388	0.3582	0.39	61
6-3	0.27	0.2970	0.3153	0.3231	0.3412	0.3588	0.36	56
6-6	0.28	0.3040	0.3166	0.3238	0.3443	0.3638	0.40	53
6-9	0.28	0.2976	0.3117	0.3223	0.3450	0.3615	0.38	56
7-0	0.26	0.2956	0.3100	0.3270	0.3488	0.3630	0.42	60
7-3	0.30	0.2998	0.3161	0.3333	0.3434	0.3602	0.40	57
7-6	0.28	0.3090	0.3193	0.3357	0.3443	0.3620	0.40	61
7-9	0.29	0.3002	0.3183	0.3428	0.3583	0.3643	0.38	49
8-0	0.28	0.3042	0.3189	0.3370	0.3569	0.3670	0.39	49
8-3	0.30	0.3046	0.3200	0.3378	0.3577	0.3643	0.42	59
8-6	0.32	0.3179	0.3236	0.3436	0.3594	0.3740	0.40	44
8-9	0.30	0.3163	0.3246	0.3428	0.3616	0.3802	0.40	48
9-0	0.30	0.3165	0.3220	0.3395	0.3603	0.3780	0.44	55
9-3	0.31	0.3174	0.3275	0.3483	0.3625	0.3795	0.42	56
9-6	0.28	0.3245	0.3355	0.3512	0.3608	0.3760	0.41	33
9-9	0.30	0.3120	0.3325	0.3500	0.3636	0.3815	0.40	42
10-0	0.30	0.3167	0.3242	0.3450	0.3600	0.3650	0.42	36
10-3	0.31	0.3213	0.3361	0.3530	0.3700	0.3890	0.40	60
10-6	0.30	0.3285	0.3433	0.3567	0.3838	0.4002	0.42	39
10-9	0.32	0.3400	0.3550	0.3621	0.3800	0.3950	0.42	27
11-0	0.30	0.3172	0.3275	0.3525	0.3636	0.3785	0.42	36
11-3	0.31	0.3340	0.3418	0.3593	0.3775	0.3976	0.40	53
11-6	0.31	0.3184	0.3325	0.3580	0.3775	0.3993	0.41	34
11-9	0.32	0.3361	0.3411	0.3550	0.3775	0.3925	0.41	33

Table 12, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
12-0	0.30	0.3256	0.3356	0.3571	0.3640	0.3973	0.43	30
12-3	0.32	0.3350	0.3450	0.3604	0.3833	0.4017	0.44	42
12-6	0.32	0.3272	0.3395	0.3544	0.3675	0.3972	0.41	42
12-9	0.32	0.3290	0.3400	0.3567	0.3683	0.3880	0.40	24
13-0	0.32	0.3310	0.3421	0.3586	0.3700	0.3890	0.40	36
13-3	0.32	0.3357	0.3500	0.3640	0.3983	0.4037	0.43	36
13-6	0.32	0.3354	0.3416	0.3586	0.3744	0.3973	0.44	36
13-9	0.32	0.3307	0.3396	0.3558	0.3812	0.3982	0.42	24
14-0	0.31	0.3368	0.3471	0.3596	0.3779	0.3913	0.40	42
14-6	0.28	0.3235	0.3425	0.3650	0.3831	0.4002	0.42	36
15-0	0.31	0.3340	0.3420	0.3650	0.3850	0.4024	0.44	36
15-3	0.30	0.3157	0.3217	0.3550	0.4000	0.4130	0.42	36
16-0	0.31	0.3370	0.3550	0.3642	0.3883	0.4024	0.44	60
17-0	0.32	0.3350	0.3444	0.3604	0.3775	0.3975	0.40	72
18-0	0.32	0.3245	0.3362	0.3588	0.3867	0.4030	0.46	36
19-0	0.31	0.3206	0.3470	0.3650	0.3950	0.4160	0.47	42
20-0	0.31	0.3240	0.3455	0.3588	0.3788	0.4182	0.44	36
21-0	0.32	0.3345	0.3519	0.3635	0.3862	0.4060	0.46	36
22-0	0.31	0.3225	0.3392	0.3600	0.3981	0.4038	0.42	24
23-0	0.32	0.3387	0.3442	0.3800	0.3960	0.4026	0.40	24
24-0	0.32	0.3185	0.3408	0.3638	0.3838	0.4027	0.44	24

the ventricular contraction, it seems reasonable that it should be useful in evaluating involvement of a large mass of cardiac muscle in inflammatory conditions such as rheumatic carditis. The accuracy of the measurement is of the same order as that for the P-R interval, and since the Q-T interval is much longer, the relative accuracy is greater. To offset these obvious advantages, the Q-T is known to vary with heart rate and under various other influences (21, 28, 32). The large number of formulae that have been advanced for correction of the Q-T duration for changes in pulse rate attests to the difficulty of precise determination of the influence of even this single cause of variability (11). Most authors have included a constant which is different for women than the one used for men and children, and many

of the equations do not correct either the very rapid or the very slow pulse rate influences. Finally, the literature contains no serial measurements taken on the same individuals in health, the only longitudinal records having been taken on children who were known either to have or to have had rheumatic heart disease. The Q-T measurements were made with the hope that a clearer picture of developmental changes within the individual in health could be delineated and that perhaps group data might further elucidate general considerations for this measurement.

Graphic standards derived for the Q-T interval in lead II are illustrated in Fig. 10 with the medians for leads I and III. It is apparent that the greater part of the increase in duration with age is complete

Fig. 10

by the increase in heart rate, but is limited by the rise in heart rate. The Q-T measurements were made with the hope that a clearer picture of developmental changes within the individual in health could be delineated and that perhaps group data might further elucidate general considerations for this measurement.

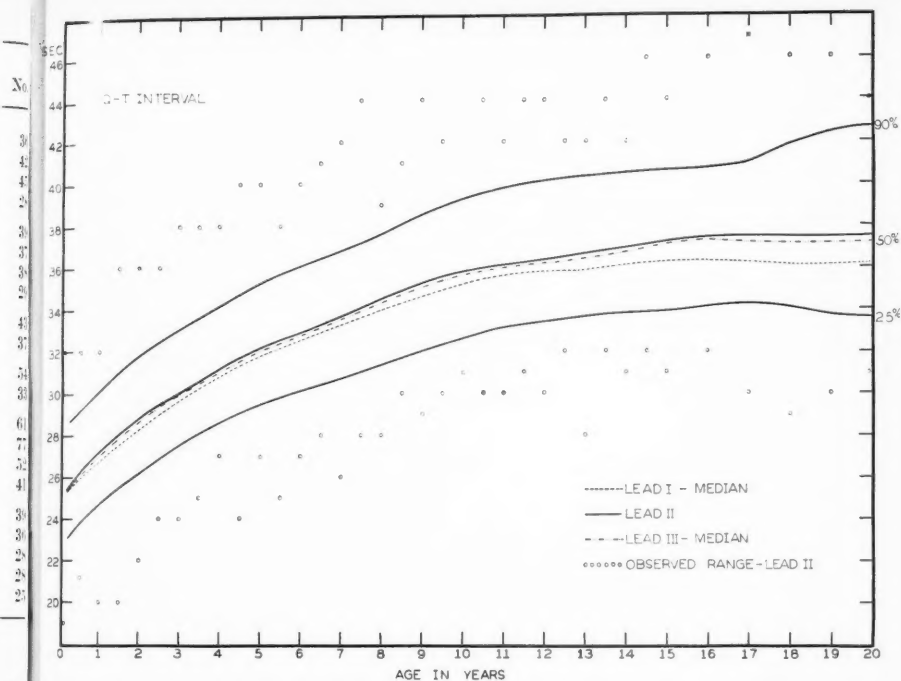


Fig. 10. Percentile standards and observed range of Q-T interval duration in healthy subjects from 2 months to 20 years of age.

by the age of 10 years. There is a gradual increase that continues to age 20, and the limited data available indicate that this rise continues at least to age 25. The abrupt and rather marked rise in the 90th percentile line after age 17 is not explained, but it is shared in lesser degree by the 75th percentile line. Upward skewing of the group data is again manifest, together with a relatively wide scatter in the upper 10% and the lower 10%. Data for the sexes separately is illustrated in Fig. 11. Women are said to have longer Q-T intervals than men (33), but this was not true in this group. In fact, the percentiles for the sexes are so nearly the same that

the differences are well within the error of measurement at any age and may be ignored.

Fig. 11 also illustrates the Q-Tc interval, corrected by the formula of Taran (26). The sex differences in the early years of life and in adolescence and young maturity which may be seen in this graph must of necessity result from differences in pulse rate, since there are no similar differences in the Q-T interval measurements. It is surprising that such small and statistically insignificant differences in pulse rate as were evident between the sexes could produce this great a variation between the sexes even at the level of the

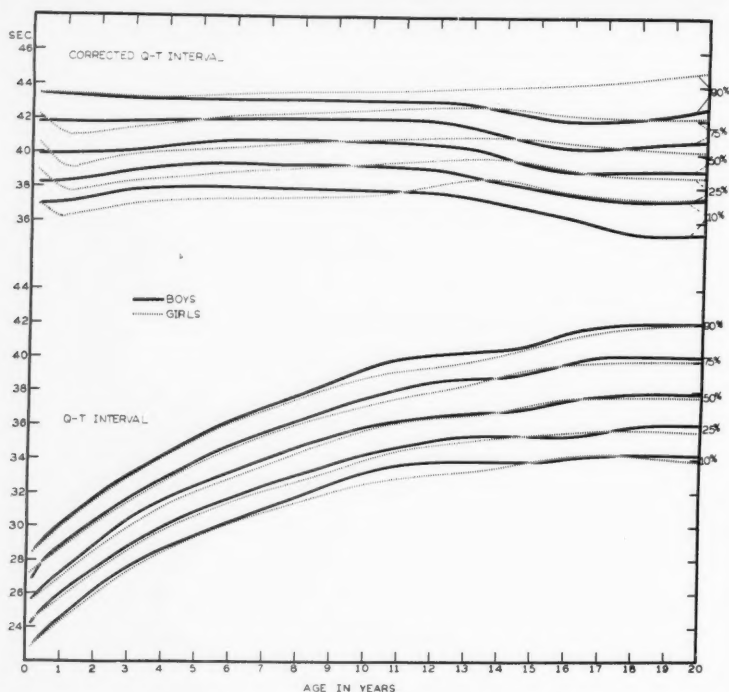


Fig. 11. Percentile standards for duration of Q-T interval and corrected Q-T interval for boys and girls, illustrating lack of sex difference in Q-T and a clear sex difference in Q-Tc. The similarity in the width of range for the two measurements is also shown.

median. The sagging of the percentile lines for boys during the ages of adolescence apparently represents a slowing of the pulse rate that is not accompanied by a proportionate prolongation of the Q-T interval, and the early sagging in the lines for the girls, while more difficult to account for, seems to arise from failure of the Q-T to lengthen in proportion to the slowing of the pulse. Individuals clearly showing either of these patterns could not be found. In any case, the attempt to correct for the influence of pulse rate results in a separation of the standards by sex, which does not occur in the basic measurements

of the Q-T interval. In addition, the range from the 10th percentile to the 90th percentile in the Q-Tc standards is no narrower than that for the Q-T standards, and at least in this group, fully 25% to 50% of the subjects exceed previously published upper limits of normal for Q-Tc duration, depending on what standards are used.

Fig. 12 illustrates the pulse rates, Q-T intervals and Q-Tc intervals for 2 boys. The hope that individuals in health might remain consistently within a part of the range for the group as they do for the P-R interval was not fulfilled. On the contrary,

Age

0-1

0-2

0-3

0-4

0-5

0-6

0-9

1-0

1-3

1-6

1-9

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2-9

3-0

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9-0

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9-9

10-0

10-3

10-6

10-9

11-0

11-3

11-6

11-9

TABLE 13. *Lead II. Percentile distribution of Q-T interval.*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No
0-1	0.19	0.2197	0.2371	0.2492	0.2624	0.2764	0.32	107
0-2	0.20	0.2354	0.2421	0.2580	0.2680	0.2852	0.32	98
0-3	0.20	0.2357	0.2497	0.2610	0.2743	0.2976	0.34	95
0-4	0.20	0.2468	0.2572	0.2700	0.2812	0.2955	0.36	43
0-5	0.20	0.2380	0.2571	0.2733	0.2825	0.2978	0.31	28
0-6	0.21	0.2368	0.2466	0.2602	0.2756	0.2835	0.32	114
0-9	0.20	0.2381	0.2496	0.2620	0.2772	0.2959	0.32	103
1-0	0.20	0.2397	0.2557	0.2641	0.2789	0.2872	0.32	108
1-3	0.21	0.2385	0.2560	0.2755	0.2888	0.3015	0.33	93
1-6	0.20	0.2433	0.2600	0.2782	0.2950	0.3163	0.36	95
1-9	0.22	0.2560	0.2645	0.2793	0.2918	0.3157	0.36	97
2-0	0.22	0.2612	0.2762	0.2835	0.3037	0.3219	0.36	106
2-3	0.22	0.2664	0.2780	0.2950	0.3043	0.3228	0.36	118
2-6	0.24	0.2692	0.2826	0.2975	0.3071	0.3213	0.36	102
2-9	0.22	0.2713	0.2824	0.2993	0.3175	0.3232	0.36	114
3-0	0.24	0.2722	0.2847	0.3024	0.3184	0.3297	0.38	112
3-3	0.23	0.2793	0.2934	0.3039	0.3199	0.3318	0.36	97
3-6	0.24	0.2810	0.2917	0.3107	0.3229	0.3390	0.38	84
3-9	0.24	0.2810	0.2944	0.3050	0.3214	0.3320	0.36	87
4-0	0.27	0.2863	0.3015	0.3160	0.3275	0.3457	0.38	88
4-3	0.24	0.2867	0.2972	0.3093	0.3218	0.3430	0.38	73
4-6	0.24	0.2958	0.3031	0.3189	0.3296	0.3460	0.40	69
4-9	0.26	0.2959	0.3060	0.3203	0.3368	0.3430	0.37	73
5-0	0.27	0.3007	0.3117	0.3217	0.3386	0.3517	0.40	72
5-3	0.25	0.2990	0.3125	0.3242	0.3419	0.3583	0.40	60
5-6	0.25	0.2905	0.3062	0.3256	0.3403	0.3622	0.38	64
5-9	0.27	0.3024	0.3172	0.3292	0.3459	0.3576	0.40	66
6-0	0.27	0.2953	0.3150	0.3283	0.3440	0.3586	0.40	62
6-3	0.29	0.3030	0.3175	0.3244	0.3488	0.3633	0.40	56
6-6	0.28	0.3110	0.3204	0.3336	0.3556	0.3632	0.41	53
6-9	0.26	0.3004	0.3150	0.3283	0.3550	0.3640	0.40	56
7-0	0.26	0.3010	0.3182	0.3336	0.3557	0.3730	0.42	60
7-3	0.20	0.3048	0.3189	0.3369	0.3538	0.3655	0.41	57
7-6	0.28	0.3060	0.3217	0.3390	0.3517	0.3633	0.44	61
7-9	0.29	0.3002	0.3200	0.3550	0.3640	0.3738	0.40	49
8-0	0.28	0.3140	0.3262	0.3439	0.3625	0.3790	0.39	51
8-3	0.29	0.3180	0.3310	0.3450	0.3617	0.3794	0.42	59
8-6	0.30	0.3232	0.3358	0.3512	0.3627	0.3807	0.41	45
8-9	0.30	0.3208	0.3379	0.3528	0.3658	0.3828	0.42	48
9-0	0.29	0.3181	0.3350	0.3490	0.3675	0.3846	0.44	56
9-3	0.30	0.3208	0.3330	0.3563	0.3650	0.3970	0.43	56
9-6	0.30	0.3247	0.3396	0.3569	0.3688	0.3860	0.42	33
9-9	0.28	0.3235	0.3403	0.3565	0.3688	0.3982	0.41	42
10-0	0.31	0.3250	0.3389	0.3517	0.3725	0.3817	0.44	35
10-3	0.30	0.3244	0.3446	0.3592	0.3735	0.3983	0.42	59
10-6	0.30	0.3380	0.3535	0.3625	0.3888	0.4024	0.44	38
10-9	0.28	0.3475	0.3550	0.3621	0.3800	0.3950	0.42	27
11-0	0.30	0.3227	0.3388	0.3591	0.3694	0.3840	0.42	36
11-3	0.32	0.3395	0.3497	0.3633	0.3835	0.3996	0.42	53
11-6	0.31	0.3240	0.3385	0.3633	0.3875	0.4032	0.44	34
11-9	0.30	0.3350	0.3440	0.3593	0.3800	0.4050	0.42	33

Table 13, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
12-0	0.30	0.3383	0.3454	0.3581	0.3775	0.3973	0.44	30
12-3	0.31	0.3390	0.3575	0.3750	0.3962	0.4038	0.44	42
12-6	0.32	0.3387	0.3552	0.3638	0.3794	0.4013	0.42	40
12-9	0.32	0.3363	0.3483	0.3607	0.3800	0.3937	0.40	29
13-0	0.28	0.3390	0.3572	0.3690	0.3825	0.3970	0.42	39
13-3	0.30	0.3390	0.3550	0.3783	0.4017	0.4206	0.44	37
13-6	0.32	0.3360	0.3525	0.3700	0.3836	0.4018	0.44	38
13-9	0.32	0.3307	0.3557	0.3618	0.3912	0.4016	0.42	29
14-0	0.31	0.3352	0.3561	0.3662	0.3834	0.4015	0.42	40
14-6	0.32	0.3363	0.3533	0.3750	0.3985	0.4036	0.46	37
15-0	0.31	0.3390	0.3510	0.3772	0.3933	0.4070	0.44	50
15-3	0.28	0.3160	0.3250	0.3600	0.3983	0.4043	0.44	24
16-0	0.32	0.3448	0.3589	0.3778	0.3962	0.4178	0.46	62
17-0	0.30	0.3508	0.3585	0.3775	0.3936	0.4026	0.47	75
18-0	0.29	0.3386	0.3556	0.3750	0.3992	0.4180	0.46	52
19-0	0.30	0.3330	0.3550	0.3783	0.4000	0.4360	0.46	41
20-0	0.31	0.3345	0.3544	0.3636	0.3839	0.4178	0.44	41
21-0	0.32	0.3398	0.3579	0.3800	0.4015	0.4260	0.46	36
22-0	0.32	0.3400	0.3556	0.3650	0.4012	0.4200	0.48	28
23-0	0.32	0.3556	0.3625	0.3888	0.3991	0.4034	0.44	28
24-0	0.30	0.3235	0.3542	0.3760	0.3982	0.4040	0.44	27

both these boys show wide fluctuations in the duration of the Q-T, which exceed in range in several instances the concomitant pulse rate fluctuations relative to the total group range. Further, while most changes in Q-T duration are in the direction that would be expected from pulse rate changes, this is not always the case, as, for example, the rise in Q-T in L. H. at age 13 years 3 months when his pulse also shows an increase. It is also apparent that a given change in pulse rate is not necessarily associated with the same amount of change in the Q-T interval at different ages. This variability in the relationship between pulse rate and Q-T duration probably accounts for the relatively wide scatter around the diagonal line of concentration in Fig. 6, together with the relatively low coefficient of correlation of minus .59 derived from that data.

The use of the Q-Tc rather than the absolute Q-T interval measurements does not lessen the fluctuations for the individual. These two representative boys both show the characteristic fluctuations seen for all the children, varying throughout the entire range observed for the group of boys. D. W. was selected because he was the only individual of the 214 children studied who showed successful correction over a significant period of time. Between the ages of 9 months and 6 years 6 months his Q-Tc represents what amounts to a straight horizontal line in spite of considerable fluctuation in both pulse rate and Q-T duration. After the age of 6 years 6 months, with certainly no greater fluctuation in pulse rate and Q-T than he had shown before, his Q-Tc shows very marked departure from his previous level, both upward and downward. It is stressed that

Fig. 12.
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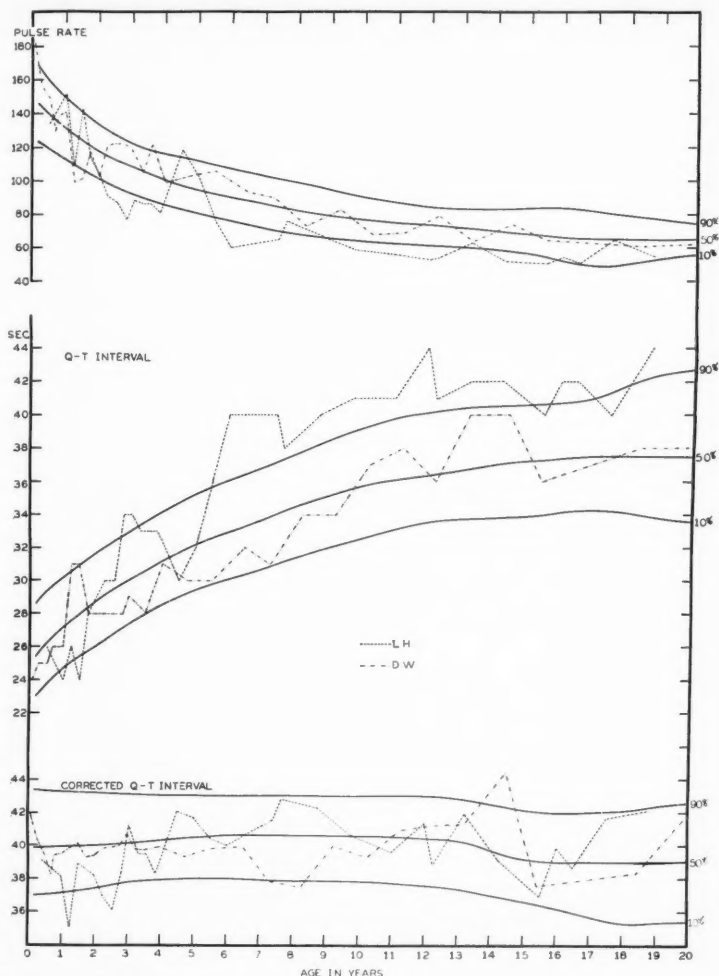


Fig. 12. Graphic representation of pulse rates, Q-T interval durations and correct Q-T intervals for 2 healthy boys, showing characteristic fluctuations of the Q-T duration and the corrected Q-T duration. Changes in Q-T duration for the most part are opposite in direction from changes in pulse rate, but this is not uniform in all instances.

only one of the 214 children did not show these fluctuations at almost all ages, which suggests that finding a relatively constant Q-Tc may in itself be a manifestation of abnormality. That is to say that while our data does not support the

concept that elevation of this derived measurement is associated with myocarditis, the possibility remains that relative fixation of this interval over a period of time may prove to be an attribute of the diseased heart with limited responsiveness

TABLE 14. *Lead III. Percentile distribution of Q-T interval.*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	N	Age
0-1	0.20	0.2179	0.2363	0.2446	0.2609	0.2795	0.30	8	12-0
0-2	0.20	0.2241	0.2393	0.2536	0.2675	0.2837	0.30	8	12-3
0-3	0.20	0.2246	0.2408	0.2568	0.2712	0.2865	0.32	8	12-6
0-4	0.20	0.2365	0.2531	0.2644	0.2803	0.2873	0.32	37	12-9
0-5	0.20	0.2240	0.2525	0.2640	0.2815	0.2905	0.30	18	13-0
0-6	0.22	0.2246	0.2405	0.2563	0.2669	0.2808	0.32	98	13-3
0-9	0.21	0.2351	0.2417	0.2583	0.2656	0.2813	0.32	89	13-6
1-0	0.21	0.2377	0.2447	0.2615	0.2760	0.2830	0.32	81	13-9
1-3	0.22	0.2389	0.2567	0.2706	0.2829	0.2968	0.32	77	14-0
1-6	0.22	0.2423	0.2587	0.2728	0.2850	0.3178	0.36	85	14-6
1-9	0.22	0.2510	0.2621	0.2791	0.2890	0.3037	0.34	82	15-0
2-0	0.22	0.2591	0.2754	0.2828	0.3013	0.3205	0.36	91	15-3
2-3	0.24	0.2621	0.2778	0.2875	0.3026	0.3201	0.34	160	16-0
2-6	0.24	0.2593	0.2768	0.2954	0.3042	0.3204	0.34	161	17-0
2-9	0.22	0.2683	0.2798	0.2966	0.3080	0.3217	0.36	160	18-0
3-0	0.24	0.2644	0.2807	0.2983	0.3158	0.3228	0.38	160	19-0
3-3	0.23	0.2756	0.2846	0.3008	0.3180	0.3246	0.36	91	20-0
3-6	0.24	0.2762	0.2848	0.3029	0.3195	0.3335	0.38	77	21-0
3-9	0.24	0.2777	0.2952	0.3071	0.3219	0.3387	0.36	81	22-0
4-0	0.27	0.2838	0.2983	0.3161	0.3244	0.3484	0.36	82	23-0
4-3	0.24	0.2720	0.2906	0.3039	0.3198	0.3315	0.38	68	24-0
4-6	0.24	0.2863	0.3000	0.3182	0.3243	0.3440	0.40	64	
4-9	0.26	0.2865	0.3012	0.3173	0.3308	0.3424	0.36	65	
5-0	0.28	0.2892	0.3028	0.3188	0.3366	0.3444	0.40	69	
5-3	0.25	0.2940	0.3095	0.3209	0.3372	0.3505	0.36	59	
5-6	0.25	0.2818	0.3069	0.3235	0.3403	0.3532	0.38	60	
5-9	0.27	0.2998	0.3167	0.3261	0.3428	0.3601	0.38	63	Age
6-0	0.27	0.2843	0.3083	0.3233	0.3404	0.3505	0.40	57	
6-3	0.28	0.3088	0.3174	0.3236	0.3469	0.3608	0.40	51	0-1
6-6	0.29	0.3120	0.3190	0.3317	0.3433	0.3622	0.40	49	0-2
6-9	0.26	0.2990	0.3172	0.3377	0.3450	0.3642	0.40	51	0-3
7-0	0.28	0.2996	0.3169	0.3308	0.3545	0.3635	0.40	58	0-4
7-3	0.20	0.3012	0.3175	0.3371	0.3580	0.3649	0.41	49	0-5
7-6	0.30	0.3168	0.3236	0.3395	0.3531	0.3636	0.42	59	0-6
7-9	0.29	0.3157	0.3228	0.3493	0.3606	0.3703	0.40	47	0-9
8-0	0.30	0.3067	0.3221	0.3405	0.3589	0.3733	0.39	49	1-0
8-3	0.29	0.3173	0.3234	0.3433	0.3631	0.3780	0.40	56	1-3
8-6	0.32	0.3228	0.3370	0.3475	0.3632	0.3815	0.42	43	1-6
8-9	0.30	0.3160	0.3250	0.3428	0.3630	0.3830	0.41	45	1-9
9-0	0.29	0.3190	0.3340	0.3436	0.3633	0.3850	0.42	53	2-0
9-3	0.30	0.3191	0.3308	0.3554	0.3753	0.3848	0.40	55	2-3
9-6	0.30	0.3213	0.3404	0.3557	0.3688	0.3860	0.42	33	2-6
9-9	0.31	0.3200	0.3389	0.3554	0.3627	0.3988	0.40	40	2-9
10-0	0.32	0.3245	0.3391	0.3500	0.3645	0.3802	0.44	34	3-0
10-3	0.32	0.3223	0.3421	0.3571	0.3650	0.3930	0.40	56	3-3
10-6	0.30	0.3230	0.3438	0.3621	0.3933	0.4016	0.44	37	3-6
10-9	0.28	0.3440	0.3569	0.3700	0.3815	0.3960	0.42	25	3-9
11-0	0.31	0.3217	0.3369	0.3550	0.3644	0.3850	0.42	33	4-0
11-3	0.31	0.3335	0.3434	0.3628	0.3802	0.3996	0.42	53	4-3
11-6	0.31	0.3200	0.3425	0.3612	0.3829	0.4000	0.44	32	4-6
11-9	0.30	0.3370	0.3483	0.3612	0.3817	0.4023	0.42	31	4-9

Table 14, cont.

N	Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
8	12-0	0.30	0.3245	0.3395	0.3558	0.3738	0.3905	0.42	33
8	12-3	0.31	0.3368	0.3552	0.3645	0.3846	0.4036	0.44	39
8	12-6	0.32	0.3364	0.3492	0.3633	0.3792	0.3880	0.42	40
8	12-9	0.32	0.3382	0.3488	0.3625	0.3825	0.3973	0.40	26
15	13-0	0.30	0.3415	0.3535	0.3712	0.3834	0.4004	0.42	36
50	13-3	0.30	0.3340	0.3531	0.3643	0.3945	0.4032	0.42	34
80	13-6	0.32	0.3455	0.3580	0.3675	0.3815	0.4022	0.44	36
81	13-9	0.32	0.3237	0.3400	0.3606	0.3825	0.3997	0.42	28
77	14-0	0.32	0.3283	0.3450	0.3632	0.3828	0.3970	0.40	42
87	14-6	0.30	0.3415	0.3571	0.3720	0.3925	0.4028	0.42	36
82	15-0	0.31	0.3363	0.3500	0.3760	0.3925	0.4157	0.46	54
91	15-3	0.30	0.2960	0.3050	0.3550	0.4000	0.4230	0.42	31
160	16-0	0.28	0.3418	0.3572	0.3785	0.3953	0.4041	0.44	60
160	17-0	0.30	0.3470	0.3568	0.3634	0.3867	0.4021	0.44	75
160	18-0	0.32	0.3390	0.3561	0.3750	0.4017	0.4363	0.47	49
160	19-0	0.30	0.3210	0.3575	0.3683	0.3850	0.4070	0.47	38
91	20-0	0.31	0.3364	0.3512	0.3644	0.3845	0.4182	0.46	39
75	21-0	0.32	0.3440	0.3606	0.3817	0.4012	0.4214	0.44	35
81	22-0	0.32	0.3395	0.3554	0.3700	0.4012	0.4155	0.42	28
82	23-0	0.32	0.3470	0.3612	0.3783	0.3975	0.4030	0.42	27
68	24-0	0.33	0.3420	0.3562	0.3700	0.3954	0.4022	0.44	25

TABLE 15. Percentile distribution of Q-Tc interval (boys).

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
0-1	0.32	0.3620	0.3750	0.3967	0.4164	0.4310	0.46	44
0-2	0.34	0.3660	0.3855	0.4009	0.4162	0.4288	0.45	45
0-3	0.34	0.3672	0.3866	0.3957	0.4192	0.4420	0.46	39
0-4	0.36	0.3650	0.3883	0.4025	0.4183	0.4300	0.49	20
0-5	0.37	0.3960	0.4088	0.4262	0.4331	0.4395	0.44	11
0-6	0.33	0.3648	0.3815	0.3945	0.4115	0.4302	0.47	59
0-9	0.36	0.3660	0.3858	0.3964	0.4217	0.4445	0.45	52
1-0	0.32	0.3660	0.3778	0.3944	0.4175	0.4297	0.45	57
1-3	0.35	0.3660	0.3788	0.3975	0.4165	0.4362	0.45	45
1-6	0.35	0.3656	0.3775	0.3967	0.4115	0.4244	0.48	43
1-9	0.35	0.3718	0.3814	0.3935	0.4096	0.4260	0.44	47
2-0	0.36	0.3771	0.3861	0.4019	0.4171	0.4327	0.46	47
2-3	0.35	0.3775	0.3880	0.4007	0.4150	0.4300	0.45	60
2-6	0.36	0.3787	0.3886	0.4028	0.4188	0.4299	0.46	56
2-9	0.37	0.3833	0.3928	0.4027	0.4196	0.4414	0.47	55
3-0	0.36	0.3814	0.3900	0.4028	0.4175	0.4286	0.45	52
3-3	0.36	0.3813	0.3952	0.4046	0.4192	0.4320	0.47	49
3-6	0.37	0.3760	0.3925	0.4050	0.4183	0.4337	0.49	44
3-9	0.36	0.3732	0.3888	0.4006	0.4122	0.4242	0.48	43
4-0	0.36	0.3705	0.3865	0.3983	0.4156	0.4235	0.45	42
4-3	0.35	0.3805	0.3897	0.4038	0.4215	0.4322	0.45	31
4-6	0.33	0.3773	0.3850	0.4010	0.4250	0.4420	0.47	36
4-9	0.34	0.3852	0.3953	0.4064	0.4162	0.4272	0.45	41

Table 15, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.	Age
5-0	0.37	0.3885	0.3973	0.4050	0.4271	0.4344	0.46	33	0-1
5-3	0.34	0.3770	0.3930	0.4117	0.4250	0.4430	0.48	33	0-2
5-6	0.34	0.3670	0.3890	0.4021	0.4170	0.4277	0.47	33	0-3
5-9	0.36	0.3952	0.4045	0.4144	0.4295	0.4413	0.49	31	0-4
6-0	0.35	0.3645	0.3862	0.4029	0.4122	0.4287	0.45	28	0-5
6-3	0.37	0.3840	0.3917	0.4083	0.4221	0.4305	0.44	28	0-6
6-6	0.36	0.3695	0.3881	0.4062	0.4225	0.4360	0.48	28	0-9
6-9	0.36	0.3690	0.3900	0.4012	0.4125	0.4237	0.43	24	1-0
7-0	0.35	0.3690	0.3933	0.4070	0.4158	0.4243	0.46	24	1-3
7-3	0.37	0.3810	0.3893	0.4072	0.4150	0.4234	0.45	28	1-6
7-6	0.35	0.3640	0.3906	0.4044	0.4212	0.4316	0.45	37	1-9
7-9	0.36	0.3855	0.3981	0.4112	0.4285	0.4348	0.44	21	2-0
8-0	0.36	0.3770	0.3825	0.4100	0.4208	0.4330	0.44	22	2-3
8-3	0.36	0.3810	0.3975	0.4150	0.4270	0.4377	0.45	32	2-6
8-6	0.37	0.3790	0.3893	0.4010	0.4150	0.4323	0.44	28	2-9
8-9	0.36	0.3790	0.3925	0.4100	0.4233	0.4343	0.46	22	3-0
9-0	0.33	0.3720	0.3908	0.4000	0.4092	0.4227	0.43	27	3-3
9-3	0.36	0.3820	0.3912	0.4067	0.4156	0.4340	0.47	31	3-6
9-6	0.36	0.3830	0.3912	0.4083	0.4200	0.4270	0.44	18	3-9
9-9	0.38	0.3830	0.3925	0.4083	0.4190	0.4270	0.43	24	4-0
10-0	0.37	0.3859	0.3893	0.3950	0.4150	0.4270	0.43	16	4-3
10-3	0.36	0.3810	0.3930	0.4038	0.4225	0.4326	0.45	32	4-6
10-6	0.37	0.3785	0.3950	0.4150	0.4250	0.4322	0.44	24	4-9
10-9	0.37	0.3770	0.3950	0.4050	0.4200	0.4290	0.43	12	5-0
11-0	0.29	0.3755	0.3881	0.4000	0.4142	0.4247	0.44	21	5-3
11-3	0.37	0.3772	0.3871	0.4092	0.4204	0.4305	0.45	29	5-6
11-6	0.38	0.3845	0.3965	0.4075	0.4204	0.4360	0.45	18	5-9
11-9	0.37	0.3780	0.3975	0.4075	0.4200	0.4320	0.44	16	6-0
12-0	0.33	0.3778	0.3856	0.4000	0.4185	0.4248	0.45	21	6-3
12-3	0.37	0.3780	0.3900	0.4017	0.4325	0.4470	0.46	26	6-6
12-6	0.37	0.3755	0.3892	0.4020	0.4144	0.4340	0.44	21	6-9
12-9	0.36	0.3645	0.3869	0.4075	0.4204	0.4260	0.46	19	7-0
13-0	0.38	0.3788	0.3845	0.4033	0.4181	0.4360	0.46	19	7-3
13-3	0.36	0.3623	0.3812	0.4067	0.4167	0.4290	0.49	22	7-6
13-6	0.35	0.3750	0.3850	0.3933	0.4075	0.4200	0.44	20	7-9
13-9	0.38	0.3820	0.3900	0.4000	0.4125	0.4203	0.42	14	8-0
14-0	0.35	0.3658	0.3730	0.3883	0.4100	0.4280	0.44	24	8-3
14-6	0.35	0.3615	0.3875	0.4020	0.4225	0.4340	0.45	23	8-6
15-0	0.36	0.3715	0.3858	0.3915	0.3995	0.4120	0.45	23	8-9
15-6	0.36	0.3755	0.3812	0.3920	0.4075	0.4240	0.50	23	9-0
16-0	0.35	0.3623	0.3730	0.3883	0.4017	0.4143	0.49	32	9-3
17-0	0.35	0.3565	0.3729	0.3920	0.4027	0.4218	0.44	43	9-6
18-0	0.33	0.3450	0.3662	0.3883	0.4125	0.4250	0.44	30	9-9
19-0	0.35	0.3650	0.3883	0.4025	0.4167	0.4217	0.42	20	10-0
20-0	0.34	0.3420	0.3606	0.3788	0.3905	0.4095	0.42	21	10-3
21-0	0.34	0.3595	0.3825	0.3925	0.4015	0.4260	0.44	19	10-9
22-0	0.36	0.3598	0.3825	0.4038	0.4262	0.4455	0.45	19	11-0
23-0	0.37	0.3703	0.3850	0.3917	0.4017	0.4320	0.44	16	11-3
24-0	0.36	0.3662	0.3710	0.3900	0.4200	0.4297	0.43	16	11-6

TABLE 16. *Percentile distribution of Q-Tc interval (girls).*

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
0-1	0.32	0.3632	0.3796	0.3954	0.4104	0.4292	0.46	63
0-2	0.36	0.3754	0.3853	0.4006	0.4262	0.4440	0.47	53
0-3	0.35	0.3688	0.3912	0.4055	0.4203	0.4380	0.47	55
0-4	0.37	0.3727	0.3988	0.4186	0.4292	0.4392	0.44	23
0-5	0.35	0.3620	0.3912	0.4100	0.4305	0.4365	0.44	17
0-6	0.35	0.3697	0.3822	0.3950	0.4100	0.4242	0.44	54
0-9	0.32	0.3652	0.3804	0.3969	0.4108	0.4228	0.45	51
1-0	0.32	0.3610	0.3711	0.3893	0.4035	0.4183	0.43	50
1-3	0.31	0.3604	0.3768	0.3894	0.4115	0.4327	0.48	47
1-6	0.32	0.3628	0.3762	0.3925	0.4056	0.4340	0.48	51
1-9	0.35	0.3675	0.3795	0.3938	0.4140	0.4383	0.48	50
2-0	0.35	0.3668	0.3845	0.3981	0.4142	0.4287	0.49	59
2-3	0.36	0.3666	0.3855	0.4006	0.4178	0.4457	0.49	58
2-6	0.34	0.3627	0.3767	0.3932	0.4070	0.4223	0.45	56
2-9	0.35	0.3680	0.3825	0.3954	0.4154	0.4360	0.47	59
3-0	0.35	0.3693	0.3833	0.3980	0.4150	0.4275	0.46	60
3-3	0.35	0.3686	0.3800	0.4030	0.4183	0.4280	0.48	48
3-6	0.37	0.3850	0.3925	0.4039	0.4221	0.4383	0.45	40
3-9	0.36	0.3675	0.3795	0.3989	0.4114	0.4220	0.45	45
4-0	0.36	0.3801	0.3882	0.3983	0.4120	0.4270	0.46	46
4-3	0.33	0.3605	0.3792	0.4010	0.4205	0.4295	0.44	42
4-6	0.36	0.3776	0.3866	0.3988	0.4179	0.4285	0.44	33
4-9	0.35	0.3610	0.3850	0.3972	0.4083	0.4310	0.44	32
5-0	0.37	0.3795	0.3920	0.4050	0.4145	0.4355	0.44	38
5-3	0.36	0.3677	0.3864	0.3983	0.4175	0.4310	0.45	28
5-6	0.35	0.3623	0.3825	0.3975	0.4183	0.4390	0.46	32
5-9	0.36	0.3758	0.3846	0.4014	0.4288	0.4400	0.45	35
6-0	0.37	0.3765	0.3931	0.4062	0.4218	0.4340	0.49	33
6-3	0.37	0.3720	0.3864	0.3983	0.4250	0.4590	0.47	28
6-6	0.35	0.3597	0.3883	0.4030	0.4190	0.4280	0.47	24
6-9	0.36	0.3810	0.3917	0.4050	0.4233	0.4326	0.45	32
7-0	0.37	0.3790	0.3888	0.4000	0.4188	0.4297	0.44	26
7-3	0.35	0.3672	0.3875	0.4067	0.4229	0.4353	0.44	29
7-6	0.35	0.3685	0.3800	0.4050	0.4217	0.4370	0.44	24
7-9	0.37	0.3840	0.3917	0.4083	0.4221	0.4323	0.46	28
8-0	0.37	0.3798	0.3888	0.4000	0.4175	0.4355	0.47	29
8-3	0.36	0.3785	0.3962	0.4075	0.4225	0.4380	0.48	27
8-6	0.36	0.3785	0.4071	0.4142	0.4325	0.4465	0.45	17
8-9	0.35	0.3803	0.3933	0.4130	0.4280	0.4370	0.47	26
9-0	0.37	0.3813	0.3904	0.4133	0.4294	0.4420	0.45	29
9-3	0.36	0.3725	0.3975	0.4100	0.4244	0.4400	0.46	25
9-6	0.37	0.3725	0.3938	0.4038	0.4275	0.4425	0.45	15
9-9	0.36	0.3610	0.3875	0.4000	0.4167	0.4260	0.43	18
10-0	0.37	0.3768	0.3825	0.4025	0.4192	0.4460	0.46	19
10-3	0.37	0.3740	0.3894	0.4057	0.4162	0.4327	0.46	27
10-6	0.38	0.3797	0.3875	0.4083	0.4300	0.4430	0.47	14
10-9	0.36	0.3625	0.4025	0.4167	0.4281	0.4338	0.44	15
11-0	0.36	0.3700	0.3869	0.4000	0.4158	0.4233	0.44	15
11-3	0.39	0.3910	0.3990	0.4093	0.4217	0.4403	0.45	24
11-6	0.34	0.3800	0.4025	0.4108	0.4212	0.4475	0.45	15
11-9	0.39	0.3935	0.4006	0.4100	0.4194	0.4265	0.43	17

Table 16, cont.

Age	Min.	10th %	25th %	50th %	75th %	90th %	Max.	No.
12-0	0.37	0.3700	0.3888	0.4100	0.4358	0.4433	0.45	12
12-3	0.37	0.3810	0.3950	0.4083	0.4317	0.4420	0.47	18
12-6	0.35	0.3863	0.3969	0.4083	0.4367	0.4427	0.45	24
12-9	0.40	0.3972	0.4006	0.4075	0.4188	0.4260	0.43	30
13-0	0.37	0.3850	0.3950	0.4070	0.4200	0.4350	0.46	20
13-3	0.39	0.3897	0.4000	0.4125	0.4300	0.4530	0.46	14
13-6	0.37	0.3930	0.3992	0.4083	0.4233	0.4470	0.46	19
13-9	0.37	0.3800	0.3975	0.4125	0.4358	0.4433	0.45	13
14-0	0.38	0.3845	0.3942	0.4088	0.4206	0.4355	0.44	18
14-6	0.39	0.3920	0.3988	0.4100	0.4267	0.4337	0.45	14
15-0	0.38	0.3892	0.3979	0.4108	0.4292	0.4422	0.45	31
16-0	0.36	0.3717	0.3880	0.4050	0.4133	0.4400	0.46	39
17-0	0.36	0.3723	0.3870	0.4017	0.4250	0.4477	0.47	32
18-0	0.35	0.3660	0.3900	0.4070	0.4188	0.4290	0.44	22
19-0	0.36	0.3772	0.3835	0.4012	0.4225	0.4695	0.47	21
20-0	0.36	0.3700	0.3883	0.3983	0.4250	0.4450	0.50	26
21-0	0.36	0.3785	0.3892	0.4067	0.4208	0.4315	0.45	17
22-0	0.37	0.3740	0.3962	0.4067	0.4142	0.4260	0.43	9
23-0	0.36	0.3780	0.3981	0.4075	0.4194	0.4242	0.47	13
24-0	0.40	0.3995	0.4058	0.4133	0.4238	0.4560	0.46	9

to whatever influences produce the characteristic fluctuations in the healthy heart.

Ashman, in publishing his equation for correcting Q-T duration for the influence of pulse (34), suggests that statistical manipulation may serve to conceal rather than elucidate relationships if it is used as a substitute for adequate data. He also states that a group of 10,000 electrocardiograms on healthy subjects with an inclusive pulse range would permit the Q-T: pulse rate curve to define itself. It is recognized that this data represents slightly less than half his recommended number and that the total number of individuals falls far short of what might be desirable. However, the extensive material available about this group makes it possible to say with unusual assurance that they are indeed healthy. Also, the observed ranges both of pulse rate and of

Q-T duration are sufficiently wide to make it doubtful that increasing the size of the group would materially increase the ranges. A scattergram of pulse rate against Q-T duration was therefore prepared. It became obvious at once that the pulse rate is relatively a much more precise measurement than the Q-T, so a class interval of 5 beats of the pulse was used in determining the median Q-T for pulse. Fig. 13 summarizes the original scattergram. It is apparent that if a straight line relationship existed, the median line of Q-T duration for pulse rate would coincide closely with the median line of pulse rate for Q-T duration. This is found to be true in the pulse range from 80 to 130, the same range that Schlamowitz gives for a linear relationship (35). The corresponding range of Q-T duration is from 0.26 to 0.36 second. The departure from linear

Fig. 13. Scattergram between pulse rate and Q-T duration.

relation above 130 beats per minute, and below 80 beats per minute, is not unusual. Other scattergrams for other pulse rates show similar departures from linearity.

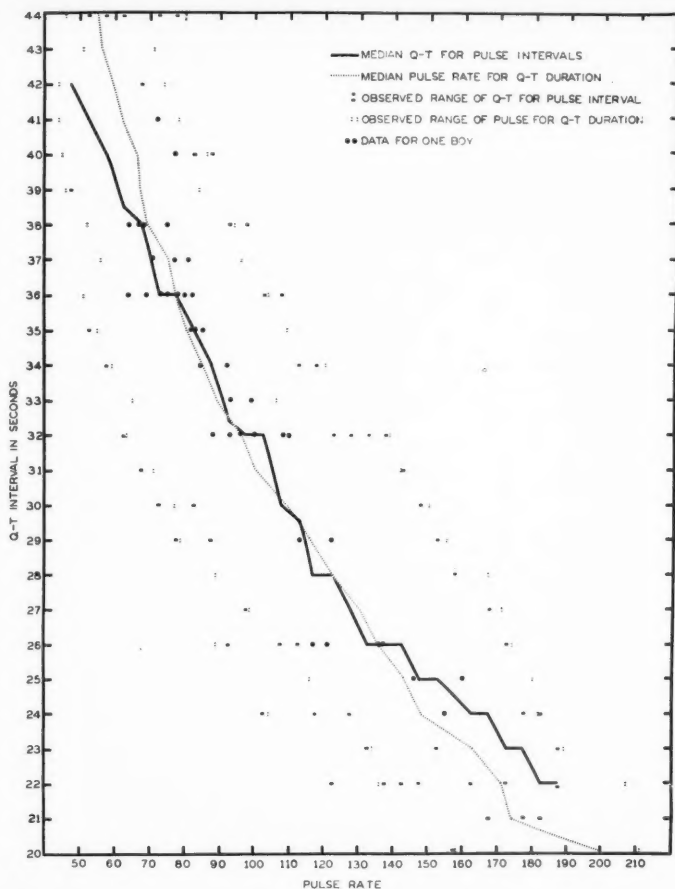


Fig. 13. Summary of scattergram of Q-T interval duration against pulse rate, illustrating difference between the median pulse rate Q-T and the median Q-T pulse rate curves. The wide scatter from the medians is also shown by the observed ranges. One healthy individual is shown to illustrate lack of linear pattern within the individual.

relationship at the more rapid pulse rates (above 130) is apparently due to the inability of cardiac conduction to accelerate beyond a given point, so the higher the pulse rises, the less relative shortening of Q-T duration can be accomplished. At the other end of the scale, even when pulse rates fail to fall, there is a rise in the dura-

tion of Q-T, resulting in an upward bowing of the median pulse rate for Q-T duration curve. Certainly the group median curves do not depart significantly from a straight line in the pulse range between 80 and 130. However, the observed ranges of Q-T duration for any given 5 beat pulse interval and of pulse rate for any given Q-T

duration are very wide indeed. With a total range of 150 pulse beats, a single Q-T duration may occur over a pulse range of 70 beats, or nearly 50% of the total range; and with a total Q-T duration range of 0.26 second, a single five-beat pulse interval can be associated with a range of 0.08 second, or essentially one-third of the total range of Q-T. The linearity of the medians is therefore of less meaning than it would be if narrower ranges existed.

The data for the individual could follow either of the two patterns. It could reflect the linearity of the medians or it could reflect the wide scatter of the total data. As may be seen from the measurement of one child shown in Fig. 13, the individual tends to scatter throughout the range observed for the group without any particular tendency to fall within a given segment of the group. Unfortunately this seems to be another example of a median relationship for the group data which has no meaning when applied to the individual.

In plotting the data for each child on the scattergram it became evident that the upward swing from the straight line seen for the median Q-T for pulse rate curve at its upper end resulted from the cumulative effect of a temporary increase in Q-T duration for each individual, which occurred some time between 17 and 22 years of age. Thus, this part of the curve represents data from a brief period in life for all those study subjects who are in their young adult years rather than reflecting a persistent pattern in a few separate people. Similarly, it is speculated that the steep rise seen in the upper percentile levels of Q-T in Figs. 10 and 11 at about this same age has an etiology associated with the

early years of maturity but is unrelated to the pulse rate.

Summary and Conclusions

Electrocardiographic interval measurements in the three standard limb leads were made on 4993 tracings taken serially from 214 healthy children from one month of age to their present ages as part of the study of human growth and development of the Child Research Council. Group standards were computed for P-R, Q-S, and Q-T interval duration in the three standard limb leads and for pulse rate and Q-Tc in lead II. Individual subjects were presented against the group background to demonstrate developmental changes in healthy subjects from infancy to maturity. Characteristic patterns of stability and instability were discussed together with their clinical applications. The following conclusions were drawn:

1. Pulse rate is a very unstable measurement during at least the first two years of life, becoming more stable after that but still showing both short-term and long-term fluctuations without obvious cause.

2. The P-R interval is a very stable measurement within the group range for any individual in health.

3. Changes in the P-R duration of more than 0.02 second on records from the same individual within any one year were not seen in the absence of illness or of obvious change in pacemaker.

4. Changes in the duration of the P-R interval which occur in the absence of disease are usually confined to one lead, while those associated with cardiac abnormality occur simultaneously in all three leads to approximately the same degree.

5. No linear relationship could be demonstrated between P-R duration and pulse rate either for the individual or in the group data. A highly significant U-shaped dependence was found between P-R duration and pulse rate for the group data. It has been speculated that this dependency resulted from some factor or factors not measured.

6. No relationship could be found between the duration of the P-R interval and heart size at a single age or between P-R duration and changes in heart size with body growth.

7. Group data for the Q-S interval duration strongly suggest that the duration of this interval is related to physical size and therefore to heart size, though conformity to a pattern corresponding to established anatomic growth curves is not universal.

8. The frequent occurrence of Q-S durations in excess of 0.10 second after 2 years of age makes this an unacceptable upper limit of normal duration.

9. The Q-T interval shows partial dependence on the pulse rate both for the group data and within the individual, but this is not uniform or predictable.

10. The corrected Q-T interval, using the square root ratio of Taran, shows as wide a range for the group data as is found for the uncorrected Q-T.

11. Individuals in health characteristically fluctuate widely through the group range for both the Q-T interval and for the corrected Q-T interval.

12. The range for the corrected Q-T interval duration extends upward far enough so that a minimum of 25% of the data falls above the previously published upper limits of normal.

13. The equation used for correcting the Q-T duration for pulse is inadequate for very fast or very slow pulses.

14. There is a temporary rise in Q-T duration between the ages of 18 and 22 years which occurs in most if not all subjects independent of rate changes.

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page 40, line 24; read: the same and as the clinical findings often overlapped.

page 70, line 19; read: patients, in 19 of whom . . .

page 100, figure 30; end of second line read: handicapped at follow-up.

page 118, table 33: Calcification, second column: for 3 read 2.

page 137, table 42; first lines of table read:

Fever of definite or possible cerebral	
origin:	23
post-S.E.G. state	1
etc.	

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JOHANNES CHRISTIAN MELCHIOR

PNEUMOENCEPHALOGRAPHY IN ATROPHIC BRAIN LESIONS IN INFANCY AND CHILDHOOD

*With special reference to the prognostic value in
non-neoplastic disorders studied by a follow-up of 271 children with
possible or definite dilatation of the ventricular system*

ARNE FROST-HANSENS FORLAG

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Denne afhandling er af det lægevidenskabelige fakultet
ved Københavns universitet antaget til offentlig at
forsvares for den medicinske doktorgrad.

København, den 14. februar 1961.

Jens Nielsen

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In memory of my father

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Copenhagen, July 1961.

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The following abbreviations are used in the review of the literature:

P.E.G. = pneumoencephalography, any form of intracranial air.
V.E.G. = ventriculography.
S.E.G. = sub-occipital encephalography.
L.E.G. = lumbar encephalography.
V.S. = ventricular system.

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CHAPTER I

Aim of the investigation

The purpose of this study was to ascertain the value of pneumoencephalography in children in diagnosing lesions other than tumours leading to ventricular dilatation.

As a result of the close collaboration between the Neurosurgical and Paediatric Departments at the Rigshospital, a great number of infants and young children have been examined, partly to exclude neoplastic lesions and partly to supplement the examination of the case. The results obtained have often had a far-reaching influence on treatment and disposal of the patient.

The present investigation has been undertaken in order to clarify several problems which have arisen, viz:

1. Is pneumoencephalography of any prognostic value and does direct measurement of the ventricular system offer any help? Can the measurements be reproduced?
2. Is there any relationship between pneumoencephalography and clinical findings?
3. Are there any special risks with pneumoencephalography and is the age at which the examination is performed of importance?
4. Is there any correlation between the pneumoencephalogram and the pathology?

CHAPTER II

Earlier investigations

P.E.G. has been in use for approximately 40 years. It has developed so rapidly that it is outside the scope of the present work to review all the literature, especially that concerning diagnostic procedures for brain tumours.

The present investigation was undertaken by a paediatrician and so it is natural that paediatric problems are given special consideration. The review of the literature includes a general survey of the development of the P.E.G. and some special aspects. As it is the first Danish monograph on pneumoencephalography it seems natural to include a review of its development in Denmark. These reviews may be subdivided as follows:

- A. The development of pneumoencephalography.
- B. The use of pneumoencephalography in children.
- C. The development of pneumoencephalography in Denmark.
- D. Methods of measuring pneumoencephalograms.

A: THE DEVELOPMENT OF PNEUMOENCEPHALOGRAPHY

The first X-ray picture of an air-filled ventricular system was obtained by *Luckett* (1913) in a patient who had sustained a head injury twenty days before, at which time air had penetrated the ventricular cavities. Similar isolated examinations were published in the next few years and for the first time in Scandinavia in 1921 by *Hansson*.

Dandy (1918) was the first to publish the results of ventriculography performed either through the fontanelle or through burr holes in 20 children between the age of six months and twelve years. This was the first intentional P.E.G. and was the outcome of a great many experiments on animals with different contrast mediums. In this report only one child developed a fever and complained of nausea and vomited following the examination. This patient was subsequently operated on for a cerebral tumour.

The following year *Dandy* published the first report of air insufflation by the lumbar route.

Widerøe (1921) from Norway and *Bingel* (1921) from Germany were the first European workers to publish their results of lumbar encephalography, a term introduced by *Bingel*.

Wartenberg (1924) appeared to be the first to mention the third major type of P.E.G., sub-occipital encephalography.

In the following decade a great many reports were published in the United States as well as in Europe and particularly in Germany. The aims of these workers were similar, viz. the investigation of the risks involved, the methods used and the therapeutic effects of insufflation.

From the United States *Martin and Uhler* (1922) published the results of 14 L.E.G.'s performed on adults and children. *Grant* (1923) had 5 deaths among 40 V.E.G.'s and in 1925 had 32 deaths among 392 V.E.G.'s. At that time he was a firm believer in V.E.G. and did not use L.E.G. at all. Later, after *Pendergrass'* report in 1931 which emphasised the great value of L.E.G., especially in children, he changed his attitude and from 1932 onwards he agreed that both methods had their particular indications and could supplement one another.

Penfield (1925) examined 60 patients and was strongly in favour of V.E.G. as well as L.E.G., and reported in 1927 good therapeutic results after lumbar P.E.G.

Pancoast and Fay (1929) surveyed the literature on the complications of P.E.G. and found 1.2% mortality in 1529 L.E.G.'s.

Considerable progress was made in Germany concerning P.E.G., its indications, complications, technical considerations etc., e.g. *Jiingling* (1926), *Heidrich* (1927), *Eskuchen* (1928), *Goette* (1929).

In addition, during the first decade, a number of reports came from Germany on more specific problems of P.E.G. *Schott and Eitel* (1922) mistrusted L.E.G., particularly the cortical findings. *Weigeldt* (1922) and *Alwan and Hirsch* (1922) reported favourable results with both V.E.G. and L.E.G. *Denk* (1922) had two deaths among 318 patients (both had inoperable tumours), and *Jiingling* (1922) in a report on V.E.G. mentioned that it was particularly easy to enter a severely dilated system by this route. *Moro* (1924) drew attention to the "splash" heard when air was injected into the ventricular system of patients with a severe degree of hydrocephalus. But he did not say that if this sign was present X-ray examination could be dispensed with.

Foerster (1929) was against S.E.G. as he found it a more dangerous procedure than L.E.G. though he did not enlarge on this. *Weber* (1929) mentioned the influence of manipulation of the head on the position of the air.

In this early period a great deal of trouble was taken to produce a normal control pneumoencephalogram, a classical example of which was *Koschewnikow's* (1926) own P.E.G. which was abnormal in that it showed absence of sub-arachnoid air over one hemisphere and slight asymmetry of the ventricular system.

In 1929 the American Roentgen Ray Society's Committee on Standardization of Encephalography stated: "It was realized that we cannot expect

encephalographic procedures to be carried out on normal individuals, and the best that we can do is to declare our judgment as to what is approximately normal from a large number of negative encephalographic studies." It can be seen from the above that there was a general increase in the number of P.E.G.'s performed and that there was universal agreement on the diagnostic value of the procedures, especially with brain tumours. At the beginning of the 1930's the last protest against P.E.G. was made by *Sahli* (1932), and in the following years was shown to be incorrect. *Sahli* states in his textbook: "Die Resultate sind so dürftig, dass das Verfahren meiner Ansicht nach mit Rücksicht auf seine Nachteile aus der Reihe der klinischen Untersuchungsmethoden gestrichen werden sollte. Es handelt sich dabei um eine gefährliche diagnostische Polypragmasie, die aus ethischen Gründen, weil der Gewinn in keinem Verhältnis zu den damit verbundenen Gefahren und Belästigungen steht, aufgegeben werden sollte." He confined his remarks on P.E.G. to fifteen lines whereas he used two pages to describe investigations with lipi odol injections.

For the next thirty years the popularity of P.E.G. tended to fluctuate. For practical purposes the literature may be subdivided:

- (a) The normal system.
- (b) General considerations.
- (c) Technical considerations.
- (d) P.E.G. experimental investigations and general reactions.
- (e) Complications and mortality.
- (f) More specific P.E.G. findings.
- (g) P.E.G. in cerebral atrophy.
- (h) P.E.G. findings in post-traumatic conditions.
- (i) P.E.G. in epilepsy.

(a) *The normal system.*

The number of publications concerning the normal ventricular system are of course limited because one would not consider applying this examination to any number of normal adults or children, and most of the so-called normal encephalograms are from patients with headaches, behaviour disturbances etc. As already mentioned, *Koschewnikow* when performing a P.E.G. on himself, found an abnormal system. In 1935 *Lysholm* in Sweden published his excellent work "Das Ventrikulogram", and also included in this is a chapter by *Sahlstedt* who states that from 300 abnormal encephalograms they tried to construct a normal model which could be used in evaluating pictures.

Heinrich (1939) examined the "normal" P.E.G.'s at different ages and found rather small ventricles in children which increased over the years. The number which he examined in the lower age group was too small to be of significance.

In 1937 *Davidoff and Dyke* published the first textbook on P.E.G., "The Normal Encephalogram", and this was followed in the next few years by similar monographs with extensive reviews, technical details and discussions of what should be considered normal. From Australia came *Robertson's* "Encephalography" (1941) and "Further Studies in Encephalography" (1946). From Germany came "Einführung in die Enzephalographie" by *Schiersmann* (1942). *Wolff and Brinkmann's* work (1940) "Das "normale" Encephalogram" will be discussed in more detail in the section on methods of measurement.

(b) General considerations.

An early review of the literature of patients with brain tumours and the diagnostic value of P.E.G. is to be found in the report of *Juželeviskij* (1931) from Russia. He had 4 deaths among 270 patients of all ages, and 3 of them occurred in children. He preferred S.E.G. to L.E.G.

Flügel (1932) from Germany, who reported his results on 603 P.E.G.'s, also preferred S.E.G. From the Mayo Clinic *Adson* (1932) preferred V.E.G. to L.E.G. *Guttmann* published an excellent review of the status of P.E.G. in the mid-1930's in *Bumke and Foerster's* "Handbuch der Neurologie," and a similar review was made by *Morea* in 1949. On the use of ventriculography in diagnosing brain tumours *Bailey* (1948) stated that: "Symptoms are exaggerated and death sometimes results from its use." He emphasised that care must be taken not to skimp the neurological examination just because one is making use of P.E.G.

In 1950 *Hodges* used the term "aerography", a term which is rarely used in English. Terminology relating to hydrocephalus was discussed by *Thiébaud and Fenelon* (1950). They suggested the terms D.V.A. (dilatation ventriculaire active), D.V.P. (dilatation ventriculaire passive) and H.O.L. (hydrocephalic occulte et latente), the latter frequently connected to D.V.A. In addition H.I.C. (hypertension intracranial) was also suggested. As far as can be seen, none of these terms have found a place in the literature.

In 1953 *Hess* from Switzerland reviewed the neurosurgical indications, techniques etc. He preferred to use S.E.G. rather than L.E.G.

(c) Technical considerations.

A great number of reports have dealt with technical considerations other than the method of insufflation. *Thorkildsen and Pirie* (1934) reported on the difficulties of interpretation of P.E.G., especially the influence of different head positions on the X-rays. *Laruelle* (1931) used only very small amounts of air (5–10 ml) for insufflation and he was supported by *Monrad-Krohn* (1933) who was initially reluctant to use L.E.G. When he employed *Laruelle's* method he found the risk of the examination (one death among 141 examined) was not high compared with the results obtained. *Ask-Upmark* (1932) emphasised the value of S.E.G., a method used increasingly in Lund since 1927.

Among 83 P.E.G.'s he had two deaths following V.E.G. but no deaths immediately after S.E.G. Two patients died twenty-four and forty-two hours after S.E.G. and in one case air failed to enter the ventricular system at all. *Schaltenbrand* (1932) reported his results of spontaneous filling of the ventricular system by suboccipital puncture. From Norway a report came which is often wrongly quoted (*Frimann-Dahl and Ingebrigtsen* 1941) who published details of a new method for lumbar and not, as quoted, suboccipital filling of the sub-arachnoid cisterns. *Kristiansen and Vogt* (1947) employed Laruelle's method of insufflating small amounts of air and found, in contrast to previous reports, that the results obtained by this technique were poor and that a considerably larger amount of air was needed if a reasonable number of pictures were to be successful. *Lemke* (1943) showed how displacement could be produced by the wrong position of the head and could be corrected by changing the position. One of the most important contributions was from *Lindgren* (1949) who emphasised the value of the fraction method of air encephalography in S.E.G. as well as L.E.G., favouring the latter method. He withdrew a few drops of cerebrospinal fluid and injected 5 ml. of air, and repeated this procedure until the required result was obtained. In this way the air was injected under pressure and he seldom used more than 25 ml.

Schiffer (1948) and *Ostertag* (1949) drew special attention to the findings concerning the third ventricle, and its relation to the clinical picture described by Kretschmer as "puberal dystrophie". The fourth ventricle was examined planimetrically by *Turner and Lutz* (1940) who emphasised how difficult it was to evaluate this on routine pictures and quoted *Twining*: "... the eye becomes lost in a maze of mastoid cells, and often encounters the back of the pinna, the outline of which can easily be mistaken for a supposed fourth ventricle."

Robertson and Childe (1940) examined the significance of asymmetry and displacement of the septum pellucidum in 84 patients who were all operated on later enabling direct examination. They conclude that if atrophy occurred after a period of rapid development there would be a tendency for the ventricular system to be displaced towards the lesion and this could be compensated by porencephaly formation or by an increased amount of sub-arachnoid fluid etc. If the loss of substance occurred during a period of rapid growth it frequently led to decreased development on the side affected.

Eaglesham (1950) found that displacement of the ventricular system was usually due either to unequal filling or to sub-dural air on the side opposite to the displacement and this latter finding was most often seen on the twenty-four hour pictures. He showed that unequal filling could be caused by bulging of the septum pellucidum to one or the other side but that it did not alter the overall picture.

The presence of sub-dural air was shown to be found in more than 50% of the 78 patients reported on by *Paul and Erickson* (1946). Sub-dural air

over the hemispheres alone was seen in 15%. These changes were particularly obvious on the second day, and it is stated that it is not unusual for the air within the first twenty-four hours to move from one ventricle to another or to the surface. This was found also by *Schatzki, Baxter and Troland* (1947) who examined changes in the size of the ventricular system on pictures taken twenty-four hours after injection, and who found that of 60 examined the size of the system increased in 23. The mechanism for the occurrence of sub-dural air was discussed by *Paul and Erickson* who felt there were two major types: (1) Incorrect positioning of the syringe so that a part of the insufflated air was introduced directly into the sub-dural space. Such a mechanism is always responsible for sub-tentorial air. (2) Ruptures of the arachnoid, among other things by tearing many of the thin adhesions over the dura, especially in the spinal cord. *Howard* (1946) indicated a technique of direct insufflation into the sub-dural space by simultaneous withdrawal of cerebrospinal fluid by lumbar puncture. He emphasised that when one finds air passing from the sub-dural space to the ventricular system there must be a communication between the sub-dural and sub-arachnoid space. In 1957 *Robertson* published one of the best monographs on P.E.G. It was primarily a survey of technical procedures and the mechanism of filling and failure to fill the ventricular system. As in his previous work, it is mainly concerned with tumour diagnosis. *Robertson* stated that S.E.G. had almost entirely been given up by most examiners because it was impossible to move the patient as much as with L.E.G. Furthermore, it was stated that the examination carried an extra risk to the patient, but he did not enlarge on this. Nevertheless, he found the method very useful in the rare case where a sub-arachnoid block was found in the spinal cord.

Reitmann (1951) draws some very drastic conclusions from very little material and his results will be discussed in the section on measuring methods. He gave the impression that he was opposed to P.E.G., a rare point of view at that time.

From France *David et al.* (1954) supported the use of L.E.G. in preference to other methods. Among 40 patients who had this procedure only one died, whereas of 23 patients who had V.E.G. 3 died. From Germany came a vast literature on pneumoencephalography: *Lennartz* (1954, 1955) preferred L.E.G. whereas *Flügel* (1955) preferred S.E.G. *Merrem* (1955) was mainly interested in the indications and found that patients over sixty years of age should not have encephalography at all, and that in children under six years of age L.E.G. should be performed. In all other age groups S.E.G. was the procedure of choice. The examination was contraindicated when the patient was unconscious and papilloedema was more than two dioptries. In cases of brain tumours V.E.G. was preferable and arteriography was an additional diagnostic aid.

Bull (1950) reviewed the use of positive contrast media for ventriculography

and included his results using small amounts of pantopaque. The only indication for this technique was when P.E.G. did not provide detailed information of the third and fourth ventricles. Trans-orbital V.E.G. was performed on 15 patients in Japan by *Wada and Toyota* (1951) without remarkable complications but the lack of further reports was against the continued use of this method. *Slosberg et al.* (1954, 1955) withdrew small amounts of cerebrospinal fluid (maximum 5–10 ml.). They found that the discomfort of the new method was less than that involved in the former technique. In discussing the publication from 1955 *Browder* stated that twenty years earlier he had insufflated 700 ml. of air in one hour without removing any fluid at all and he thought that the air was absorbed by the blood. According to *Aird and Zeale* (1950) lack of absorption of air can be seen in cases with blockage of cerebrospinal fluid production, e.g. tumours and post-infective disorders. *Jirout* (1956) found that because of oedema, caused possibly by the air, pictures of the ventricles could be judged best twenty-four hours after insufflation and for the same reason filling of the sub-arachnoid space was less complete shortly after insufflation.

The question of unsuccessful filling of the ventricular space was dealt with by *Kehrer* (1950) who found the following types: (1) No air in spite of a good position of the syringe. In all his cases this was due to tumours or tuberculosis. (2) Filling of the sub-dural space but not the ventricular system; in such cases the syringe was not inserted far enough. (3) Filling of the sub-arachnoid space or sub-dural space and partial filling of the ventricular system could be due to abnormal conditions in the cisterns, a wrong position of the head or a too shallow insertion of the syringe.

Scheinberg and Yahr (1955) examined the same problem in 2641 P.E.G.'s and found unsuccessful filling in 175. Of 95 patients with no filling of the ventricular system 70 were re-examined and of these 34 had cerebral tumours. Of 83 patients with partial filling 12 were re-examined and 4 were found to have tumours. *Martin and Gurdjian* (1953) found that among 200 patients with space-occupying lesions 18% had had previously negative examinations and they give examples and combinations of findings.

Epstein and Epstein (1958) emphasised the value of taking a picture after insufflation of 10–20 ml. of air. If air is seen sub-tentorially and/or sub-durally it is necessary to re-puncture two intervertebral spaces above. *Etter and Youngue* (1958) also found it of value to screen the patient after small insufflations especially in epileptic patients. One of the latest reviews has come from Brazil where *Rodrigues and Albernaz* (1959) mention the use of helium and removal of small amounts of cerebrospinal fluid, and in 13 of their cases describe insufflation of helium without removal of cerebrospinal fluid.

(d) *P.E.G., experimental investigations and general reactions.*

The first report on experimental work on the physical principles of encephalography was published by *Schube* (1934). He was especially interested in the pressure and temperature of the air and drew attention to the fact that when air is changed from room to body temperature, there must be an increase of pressure.

v. Storch et al. (1940) performed experimental investigations on 20 patients and noted the time of onset of headache following insufflation of small amounts of air, 1-2 ml. each time. The stage at which headache occurred was found to vary from 2-6 ml. of insufflated air and was independent of variation in pressure. It was shown that the sensitive areas were the cisterna magna and possibly the third ventricle whereas the lateral ventricle was insensitive. In cases of localised pain the authors felt that they were dealing with a meningeal reaction due to a chemical or mechanical cause and not to distortion of the vessels.

As another possible cause of headache and longer-lasting complaints following P.E.G. *Turner and Brody* (1941) described two patients in whom air remained in the ventricular system 3 and 8 weeks after insufflation. They treated this with administration of 90% oxygen and 10% CO₂ with very rapid subjective improvement.

Robertson (1941, 1946) constructed models of the ventricular system in order to have a better understanding of the filling processes. Similar experiments were performed by *Müller* (1955) who was interested in the lack of filling of the ventricular system. The hypothesis was that filling of the ventricular system was dependent on intake when one had withdrawn a little cerebrospinal fluid and if an air bubble obstructed the aqueduct air would enter the cisterns and the sub-arachnoid space. Müller states that the volume of cerebrospinal fluid withdrawn must be compensated by changes in the circulatory system and this compensation can equal a maximum of 40-50 ml.

Besides experimental work, a number of reports have been published concerning reactions to P.E.G. *Bohn* (1937) analysed 1000 consecutive L.E.G.'s and found that the majority had a slight increase of temperature after insufflation. There were two deaths and both occurred in patients with cerebral tumours.

Abeles and Schneider (1935) investigated electrocardiographic changes during P.E.G. examination in 20 patients and found severe changes related to stimulation of the pacemakers of the heart. The changes were reversible though there was one death which the author felt was due to cardiac failure, pronounced bradycardia and collapse. *Kaunisto* (1941) was unable to demonstrate changes of any importance on the electrocardiograms performed at the same time as S.E.G. except for a few small changes of the P-wave which became normal within an hour.

Delay et al. (1944, 1945 c) dealt with the biological syndrome of air encephalography. They found neurovegetative changes with brachypnoea, bradycardia, rise in blood pressure and temperature. Furthermore there was leucocytosis, decreased diuresis, hyperglycaemia, an alteration of the blood pH towards an acid reaction and, in addition, a few cells in the cerebrospinal fluid.

Kautzky and Burchard (1950) examined the so-called central fever reaction in relation to the febrile reaction following P.E.G. and were unable to come to any conclusions concerning such a connection. *Kuhlendahl* (1950) found that the vegetative reaction to P.E.G. did not have its origin in the area around the third ventricle but found that the influence of the pia, especially the pia vessels, played a major role.

Frowein and Harrer (1950) examined a great number of tests of vegetative function at the time of P.E.G. and found that the reaction could be divided into a sympathetic phase followed by a parasympathetic phase. These findings were independent of filling of the ventricular system. They suggested a pre-formed unspecific vegetative standard reaction which appeared after a short stimulus and a change in the motor function of the vegetative centres depending on the degree of filling of the ventricular system and the sub-arachnoid space, as the result of a strong stimulation.

Weinberg et al. (1950) examined 10 adult patients and found a period of decreased diuresis, decreased sodium and potassium content of the urine and frequent E.C.G. changes. In most cases erythrocytes and a few leucocytes were found in the urine in the antidiuretic phase, and in a single case albuminuria. The changes were less pronounced after V.E.G., probably because this form of examination was the least painful.

Boudin, Barbizet and Leprat (1954) examined what they called the diencephalic-endocrine reaction to P.E.G., viz. reduced diuresis, rise in temperature, disturbance of sleep, leucocytosis, changes in the blood sugar (often in the form of hyperglycaemia), changes in sex hormone function (galactorrhoea, amenorrhoea), and an increased function of the thyroid gland as shown by an increased I^{131} uptake. The authors found that these reactions were so characteristic that P.E.G. should be added to the examinations of function of the diencephalic pituitary apparatus. An increased excretion of 17-hydroxycorticoid following P.E.G. was demonstrated by *Lieberman and Luetscher* (1957) and *Wise et al.* (1958). Changes in spinal fluid during P.E.G. were seen by *Bickerstaff* (1950) who found that in 66 out of 68 patients showing an increased number of cells, 50 showed this increase within ten minutes. If an increased number of cells was present in the cerebrospinal fluid before the examination, the elevation was more pronounced. He found that these changes occurred more rapidly with children than adults. He thought this was due to an alteration in intracranial pressure, and not to removal of fluid or irritation by insufflated air.

Zarling (1951) found only slight changes in the E.E.G. during performance of L.E.G. in 11 patients and these changes disappeared within a few hours. Similar results were obtained by *Leonhardt* (1955) in 50 cases persisting for 2-6 days.

(e) *Complications and mortality.*

A survey of mortality in a number of reports, including paediatric reports, is found in Table 1, p. 26. Discussion will be confined to a brief survey of the literature on this subject and on the complications other than rise in temperature, headache and other minor reactions.

Air embolism may be a serious complication and this had been emphasised by *Begtrup-Hansen* at a discussion of *Jessen's* lecture in 1930 where he drew a parallel to the risk with pneumothorax. *Rupilius* (1934) was able to demonstrate air embolism as the cause of death in his material and *King and Otenasek* (1948) found air embolism at autopsy on two occasions immediately after L.E.G. Since then air embolism has been described by several authors, *Coleman et al.* (1950), *Heppner* (1952), *Jacoby et al.* (1959). *Sachsenweger* (1957) drew attention to localisation of the embolus to the eye where changes could be seen at an early stage and thus be a guide to treatment. Haemorrhages in the neighbourhood of a tumour were described in 3 cases by *von Streng* (1949) together with two cases of abscess formation in the puncture canal.

Whittier (1951) found a mortality of 0.28% in 2490 examinations over a six-year period. In all fatal cases a brain tumour was present.

Holub (1953) described a 49-year-old patient who died shortly after V.E.G. A haemorrhage was found completely filling the ventricular system with blood and it was impossible to find any large leaks in vessels. With regard to the pathogenesis the author found the patient had hypertension and drew attention to the possible risk of haemorrhage due to changes in pressure.

Laux (1956) found in approximately 12000 examinations 7 patients who had died of cerebral haemorrhage as a result of the examination. In all fatal cases supratentorial tumours were present.

A comparison between the frequency of complications and the different types of examinations was performed by *Albrecht* (1956) who found a mortality of 0.22% for arteriography and 8.3% in brain tumour patients studied by V.E.G. and 0.3% after S.E.G.

A most interesting case was published by *Robinson* (1957). A 48-year-old man had right-sided arteriography and 4 days later L.E.G. was performed which showed normal conditions. Over the next 3 weeks he became sleepy and dull and on examination was found to have a sub-dural haematoma of approximately two weeks' duration. *Robinson* states that one must not be misled by a normal P.E.G. but must bear in mind the possibility of abnormalities developing at or after the time of the examination.

Table 1

More important references to mortality following P.E.G.

Author	Year of publication	Material (age if specific group)	Diagnosis (if specific group examined)	No. of examinations	Type of P.E.G.	No. of deaths	Mortality in %
Denk.....	1922			318	V.E.G.	2	0.6
Mader.....	1923	child		20	L.E.G.	1	5.0
Grant.....	1923	adult	tumours	40	V.E.G.	5	12.0
Grant*.....	1925	adult?	tumours	392	V.E.G.	32	8.2
Heidrich*.....	1927			895	L.E.G.	6	0.7
Pancoast and Fay*...	1929			1529	L.E.G.	20	1.2
Juželevskij.....	1931			270	S.E.G.	4	1.5
Grant.....	1932			160	V.E.G.	10	6.2
				325	L.E.G.	1	0.3
Ask-Upmark.....	1932			15	V.E.G.	2	13.0
				50	S.E.G.	2	4.0
Monrad-Krohn.....	1933			183	L.E.G.	1	0.5
Rupilius.....	1934	child		244	L.E.G.?	1	0.5
Lemerc and Barnacle..	1936	adult?		800	L.E.G.?	12	1.5
Bohn.....	1937			1000	L.E.G.	2	0.2
Davidoff and Dyke...	1937			4000	S.E.G., L.E.G.	9	0.2
Wolff.....	1938	child		102	L.E.G.	1	1.0
Levinson.....	1947	child	oligophrenia	800	L.E.G.?	3	0.4
Magnussen.....	1950	adult	psych. illness	173	S.E.G., L.E.G.	1	0.6
Anderson.....	1951	child	mainly oligophrenia	400	L.E.G.?	6	1.5
Whittier.....	1951	adult		2490	?	6 (24)	0.2
Schuleman.....	1953			572	L.E.G.?	3	0.5
David et al.....	1954		tumours	40	L.E.G.	1	2.5
				23	V.E.G.	3	13.0
Vesterdal et al.....	1954	child		214	L.E.G.	1	0.5
Slosberg and Bornstein	1955	adult		84	L.E.G.	3	3.6
Laux.....	1956			approx. 12000	?	7	0.06
Albrecht.....	1956		tumours	241	V.E.G.	20	8.3
				302	S.E.G.	1	0.3
Charash and Dunning	1956	child	oligophrenia and epilepsy	181	L.E.G.	2	1.1
Jacoby et al.....	1959			1196	?	6	0.5

* Other examinations as well as the author's material are included.

Solomon and Barron (1957) drew attention to the risk of performing P.E.G. (presumably in the form of L.E.G.) in patients who suffered from disorders of the internal carotid artery, and based this on two cases in which hemiplegia, aphasia and hemianopia developed shortly after examination with permanent damage in one. The same point was emphasised by Dodge *et al.* (1954) who reported a case of death from similar causes.

The association between gastro-intestinal bleeding and ulceration and intracranial disorders was shown by French *et al.* (1952) experimentally, and

clinically by *Dalgaard* in several reports, the last in 1960. In the literature only a single report was found in which complications have been related to P.E.G. *Michaux and Cirilli* (1956) reported two cases, one with haematemesis and the other with melaena.

A peculiar complication was found by *Falk* (1951). Out of 203 patients who had V.E.G.'s performed, he found on repeated skull X-ray from one month to 15 years after the insufflation calcification in 27 patients. In 18 of them the calcification was in the immediate neighbourhood of the burr hole and in 9 was localised to the track of the syringe. This finding has not been reported by anyone else, and one must assume that it was an isolated observation.

As can be seen from the above, the number of complications was not great and presumably the greatest risks were haemorrhage and embolism.

(f) *More specific P.E.G. findings.*

Before considering the better established clinical entities, a number of reports of special findings will be discussed. In the late 1930's *Bannwarth* published a very extensive work on the P.E.G. findings of brain malformations. He reported 5 patients with fused lateral ventricles and 7 cases with malformations of the septum pellucidum (6 cases of cysts and one with agenesis of the septum). He stated that this diagnosis could only be made on P.E.G. and was unable to find any characteristic clinical picture.

In a few papers on P.E.G. findings in extra-pyramidal disorders *Goodhart et al.* (1936) and *Putnam and v. Storch* (1938) found a number of cases with increased amounts of air in the third ventricle and basal cisterns.

In 1948 *Kehrer* described small ventricles which led to the term "micro-ventriculie." Examination of normalities of the cerebral midline was reported by *Echternacht and Campbell* (1946) who found two major types: (1) Cysts of the septum pellucidum (5th ventricle) and the cavum Vergae (6th ventricle), and (2) Agenesis of the corpus callosum. The authors emphasised, as previously, that this diagnosis could only be established on the basis of P.E.G. The consequences of pre-frontal leucotomy were described by *Meschan and Scruggs* (1951) who found severe changes in all 19 patients examined. Porencephaly was found more frequently among patients who had dilated anterior horns before operation. *Kehrer* (1953) described the anatomy of hypochondriacal conditions in 40 cases. He found a normal ventricular system in 8 and dilatation in 29. In 34 the sub-arachnoid space was dilated most often in the parietal region.

Melot et al. (1953b) reported two cases of cranial lacunae (Lückenschädel) and severe dilatation of the ventricular system in which there appeared to be an absence of septum pellucidum in both cases. *Sifontes et al.* (1957) found if patients suffering from tuberculous meningitis did not react adequately to spe-

cific treatment, then P.E.G. should be undertaken and the basal cisterns examined in particular.

Recently the P.E.G. changes in myotonic dystrophy were reported, and *Refsum et al.* (1959) found that dilatation of the third and lateral ventricles was the most important finding.

(g) *P.E.G. in cerebral atrophy.*

Some reports were concerned with the special value of P.E.G. in atrophic lesions. *Alpers* (1936) discussing atrophy of the frontal lobe described a case of a 48-year-old man in whom atrophy was found on P.E.G. but could not be found at autopsy two years later. However, there was a two centimetre layer of fluid over the frontal lobe. His conclusion that: "The encephalogram may be said to be of value only if it conforms with the rest of the clinical evidence" may be too pessimistic.

Chodoff et al. (1948) found in patients with pre-senile dementia that P.E.G. did not help in the differential diagnosis between Pick's and Alzheimer's disease. *Murphy and Arana* (1947) collected 15 patients with cerebellar atrophy and stated that sub-tentorial air alone was not sufficient to establish the diagnosis, that there had to be large amounts of air behind as well as above the cerebellum. *Delay et al.* (1945 a, b) found a close correlation between the degree of ventricular dilatation, cortical atrophy and the degree of general paralysis.

In the textbook by *Davidoff and Epstein* "The Abnormal Encephalogram", the following is said about cerebral atrophy: "Examples of these various conditions as seen in the pneumoencephalograms, are not very numerous and indeed, are becoming fewer in recent years. The reason is a very obvious one, namely that the information to be obtained from pneumoencephalographic studies in typical examples of these various cases, is not very useful."

A great number of publications in the 1950's dealt with P.E.G. findings in brain atrophy, e.g. *Lindgren* (1951) who discussed possible errors of technique and photography etc. He stated, following his experience, that there was a certain relationship between the cranial diameter and the size of the lateral ventricles. If asymmetry was present, the largest ventricle was most often found in the largest hemisphere, but this was not so if it was due to a unilateral lesion because in this case the most dilated ventricle would be in the smallest hemisphere. *Melot and Potvliege* (1953a) used a very broad definition of atrophy and discussed asymmetrical findings. They emphasised that with atrophy asymmetry tends to move towards the side of the lesion, whereas with a tumour it moves to the opposite side. *Huber* (1953) reported 6 cases with simultaneous atrophy and schizophrenia. *Plum* (1953) examined the correlation between diffuse cerebral atrophy as shown by P.E.G. and the neurological changes and found only slight correlation except in cases with severe P.E.G. changes. *Gosling* (1955) found in 68

patients over 45 years of age with dementia that 85% showed atrophic changes on P.E.G.

Balestrieri, Greenstein and Strauss (1955) examined the relationship between E.E.G.'s and P.E.G. in established atrophy. They found in 100 patients normal E.E.G.'s in 49, symmetrical changes in 26 and asymmetrical changes in 25. There was no correlation between E.E.G., pathology and degree of dilatation. All their patients with severe E.E.G. changes in the form of foci with irregular delta activity had epilepsy and the authors emphasised that if this was not the case a tumour should be strongly suspected.

Lönnum and Engeset (1957) described a variable clinical picture with cerebral atrophy as well as variable P.E.G. findings and a relationship was found between the degree of dilatation and the severity of the disease. *Laane et al.* (1957) examined the findings in 100 patients from an adult psychiatric department. In 94 successful P.E.G.'s there were changes in 70. In patients with no E.E.G. changes there were a high number with normal P.E.G.'s. The same was true of patients who had no abnormal neurological signs.

Bruijn (1959) published an extensive work on P.E.G. findings in cerebral atrophy containing a detailed review of the literature on this subject, p. 55.

(h) *P.E.G. findings in post-traumatic conditions.*

The value of P.E.G. in post-traumatic conditions has been reported on several occasions, among others by *Monrad-Krohn* (1931), *Friedman* (1932), *Hauptmann* (1932), *Travers* (1937). *Penfield and Norcross* (1936) mentioned sub-dural traction and the post-traumatic headache, and described the method of direct insufflation into the sub-dural space.

The presence of sub-dural air has been the subject for special examination by *Lemerc and Barnacle* (1936) who analysed 800 encephalograms and found a mortality of 1.2% in a group with sub-arachnoid air as compared with 3.1% with sub-dural air. They found that sub-dural air led to more frequent and more severe reactions than sub-arachnoid air.

Mayfield and Bell (1944) found that after a head injury asymmetry of the ventricular system was the most common finding and that cortical atrophy was only of significance when there was dilatation of the ventricular space. *Troland, Baxter and Schatzki* (1946) found among 129 patients that less than 50% had abnormal P.E.G.'s as well as definite clinical changes, that approximately 25% had abnormal P.E.G.'s alone and about 10% abnormal clinical pictures.

Post-traumatic conditions were dealt with by *Klaue* (1950) who among 165 patients found 46% with diffuse dilatation of the ventricular system of which more than half were moderate to severe dilatations. *Falk and Silfverskiöld* (1954) found in 72 cases of post-traumatic headache pathological P.E.G. findings in 52 whereas in 58 patients who had headache for another reason there were abnormal findings in only 19 cases. *Aronson and*

Ransohoff (1955) described that a characteristic P.E.G. finding with extra-dural haematoma in the posterior fossa was a comma-shaped impression in the cisterna magna. Sub-dural haematomas have been dealt with by several others, e.g. *Browder et al.* (1955) who found that regional oedema of the cerebrum underneath the haematoma was the most frequent finding but this was denied in the discussion by others who found that there was a shrinkage in this area. *Gitlin* (1955) in 18 patients showed that the sub-dural fluid was closely related to blood and its presence must be due to extravasation through damaged capillary walls. *Heppner* (1960) mentioned the chronic juvenile sub-dural haematoma and emphasised the value of arteriography.

(i) *P.E.G. in epilepsy.*

P.E.G. changes in epilepsy were described by *Notkin* (1931) who among 17 adult women with epilepsy found no correlation between P.E.G. and the severity of the disorder. In all patients there was a meningeal reaction following examination. In contrast to this *Gross* (1931) found a relationship between the degree of dilatation and the clinical condition. *Boening and Konstantinu* (1933) were unable to prove such a relationship and they found that the longer the disorder lasted, the more severe were the changes.

Larsby and Lindgren (1940) examined male hospitalised epileptics between 13-61 years and were unable to demonstrate a relationship between the mental condition and the P.E.G. *Bollea* (1941) examined 100 patients with epilepsy and found all types of P.E.G.'s, viz. small, normal and dilated ventricles. *Dickerson* (1942) examined 286 P.E.G.'s of institutionalised epileptics and found that not only was such an examination an additional aid to diagnosis but it was also of particular value when the question of continued hospitalisation was being discussed with patients' relatives to have confirmation of the presence of severe changes. *Dickerson* and *Bollea* were very sceptical regarding the therapeutic effect.

Merritt and Brenner (1944) reported 3 cases of convulsions with normal P.E.G.'s who, one and a half, four and six years later, were found to have brain tumours. *White et al.* (1948) stated in their paper on focal epilepsy that all their patients had had P.E.G.'s but gave no details.

In 1952 *Marshall and Whitty* found that adults with epilepsy and abnormal findings on neurological examination often had an abnormal P.E.G. as well, whereas in 52 patients who were normal on neurological examination 51 had normal P.E.G.'s.

Schuleman (1954) in a series of 510 patients of which 69.9% had convulsions found that although P.E.G. had provided no useful information, the examination was absolutely necessary in order not to miss a tumour. *Martin and McDowell* (1954) drew special attention to the value of P.E.G. in patients with focal disorders. *Decker and Nagel* (1957) in two years examined 520 patients suffering from epilepsy by S.E.G. or by L.E.G. They

found 3% had tumours and 22 patients had characteristic dilatation of the third ventricle but there was no definite clinical entity associated with this dilatation. In cases of unilateral dilatation they found E.E.G. changes on the contralateral side. In the whole material 46% had normal P.E.G.'s and 35% had slight dilatation. *Guest and Jones* (1958) considered the value of P.E.G. in 175 adults with epilepsy and headache. Among 114 who were normal on neurological examination one had a tumour. In the remaining 61 patients there were 16 tumours. They stated that they would hesitate to perform P.E.G. if the other examinations were negative. P.E.G. findings with convulsions have been reported by *Vinken et al.* (1958). In this report it was the degree of dilatation which particularly interested the authors, and this as well as the work of *Krischek* (1959) will be discussed on p. 54.

Borenstein, Dabbah and Metzger (1959) examined the value of skull X-ray, P.E.G. and E.E.G. in 100 mentally retarded patients with convulsions, and compared the changes with 50 retarded patients without convulsions. In the 100 patients they found 60 with normal P.E.G.'s and in the 50 they found 39. Furthermore, they examined the distribution of abnormal findings in relation to the degree of mental retardation and found that the lowest I.Q.'s represented the group with the relatively highest number of normal P.E.G.'s but the numbers in each group are too small to be significant.

This general review of the literature of P.E.G. during the past forty years is not meant to be complete, as already stated in the introduction. For further information regarding tumours, conditions with increased intracranial pressure, technical problems etc. a large number of informative textbooks have been published during the past twenty years, e.g. *Davidoff* and *Dyke's "The Normal Encephalogram"*, *Robertson's "Encephalography"*, *"Further Studies in Encephalography"* and *"Pneumoencephalography"*, *Schiersmann's "Einführung in die Enzephalographie"*, and *Davidoff and Epstein's "The Abnormal Pneumoencephalogram."*

B: USE OF PNEUMOENCEPHALOGRAPHY IN CHILDREN

Since the examination was introduced it has been widely used among children. *Dandy* (1918) in his first publication dealt with children below 12 years of age and in a later work on L.E.G. 50% of the material was children. In his earlier work it was primarily children in whom there was a suspicion of a tumour and it was the same in the case of *Martin and Uhler* (1922) who reported a series of L.E.G.'s performed on children and adults.

For practical purposes this review is divided into sub-groups as follows:

- (a) Normal ventricular system in children.
- (b) General considerations.

- (c) Reactions to P.E.G. in children.
- (d) Complications and mortality.
- (e) Special findings and considerations.
- (f) P.E.G. and autopsy findings.
- (g) P.E.G. in brain-damaged children.
- (h) P.E.G. in epilepsy.
- (i) P.E.G. in cerebral palsy.
- (j) P.E.G. and mental retardation.
- (k) P.E.G. and prognostic considerations.

(a) *Normal ventricular system in children.*

Reports of the normal ventricular system as seen on P.E.G. are even more rare in children than in adults. Göllnitz (1951) described what he called "the normal child encephalogram." He discussed the difficulties associated with P.E.G. in the lower age groups, restlessness, changing size due to growth etc. His material was confined to child psychiatric patients and, as in a later work, it was the relationship between P.E.G. and motor and psychological development which he was primarily concerned with in his investigations. He found he could establish four possible deviations from normal: (a) Absent or partial filling of the ventricular system on at least two examinations, (b) Variations in the filling of the cisterns, (c) Changes in the size and (d) Changes in the shape of the ventricles. He used the measuring methods which are discussed in detail later, p. 52.

Brenner (1952) reported the results of investigating 13 children between 3 months and 3 years with apparently normal central nervous systems. He found the smallest infants had a relatively large ventricular system and drew attention to the size of the third ventricle.

In 1941 Durand and Scagliotti published their studies on P.E.G. in infants, but unfortunately the number of children studied is not recorded, so that the figures given must be considered with this reservation. In a series of publications from Norway Eek describes what he considers is a normal ventricular system, and this is discussed later, p. 57.

(b) *General considerations.*

As mentioned in the introduction a number of earlier reports were concerned with children. Mader (1923) published the result of 20 L.E.G.'s in presumably small children and recorded one death. He gave the impression that he would have preferred to use V.E.G. but that was not the departmental policy.

Knoepfelmacher (1924) was just as much in favour of the examination, not only because it taught the examiner a great deal about the condition of the brain but also because of the possible therapeutic effect in certain forms of hydrocephalus.

The first German monograph on the use of P.E.G. in children was published by *Brehme* (1926) and similar monographs appeared in subsequent years. His material consisted of 45 children of whom 44 had had L.E.G. The complications were the usual ones and the fever was seldom more than 39°C . In order to ascertain just how dangerous the procedure was, he followed the children for approximately one year and found that out of 41 patients 7 had died, 7 were healthy or had improved and 27 were unchanged. He concluded, therefore, that the examination held no special dangers.

In a paper dealing with children as well as adults published by *Koschewnikow and Fränkel* (1927), 250 patients were examined over a period of 5 years and 150 were less than 14 years of age. They were satisfied with the results obtained and considered it was a relatively safe procedure. The series of monographs from Germany was continued by *Eckstein* (1927) who examined 105 children by S.E.G. without serious complications. His material was made up mainly of tumours and post-infective conditions.

In 1936 *Law* studied 121 children by L.E.G. and obtained successful filling in 75%. There were no fatalities or reports of deterioration in the condition, and he recorded only minor complaints after the examination.

Among 102 children examined by L.E.G. by *Wolff* (1938) he reported one death, a mongoloid child who had convulsions. His material consisted of 38 children with cerebral palsy of whom 22 had dilated ventricular systems; 22 had epilepsy and of these 7 had dilatation. Of 15 patients with oligophrenia 7 had dilatation and 9 an increased amount of surface air.

Casamajor, Laidlaw and Kozinn (1949) examined 500 children and found that there was no real connection between intelligence and the degree of dilatation of the ventricular system. Nevertheless, the figures showed that among patients with low I.Q. there was a higher proportion of atrophy. They concluded that the examination was of no value to the neurologist and could only be of interest to the neurosurgeon. On the question of mental retardation and P.E.G. they said: "It is of little practical importance to know what sort of a brain, as shown by pneumoencephalography, a mentally defective person has; that is the brain with which he must go through life, and gas studies will not alter the prognosis or treatment in the slightest."

Schneider (1946) suggests a rather unusual advantage of P.E.G. in children, in that it is of value in this age group where case histories are often difficult to obtain, objective examinations difficult to perform and results often uncertain.

In 1951 *Anderson* reported a series of 400 children who had had P.E.G. He was a great believer in this investigation, even though he emphasised the risk of undertaking it without sufficient indications and experience. He found it was a relatively simple and safe procedure of considerable value.

P.E.G. was used in a great number of different diseases in childhood by *Charles and Boineau* (1954). In their preliminary report 60 patients were

examined without serious complications. A review of the therapeutic possibilities the neurosurgeon can offer the paediatrician was given by *Wertheimer and Juvet* (1954). They discussed hemispherectomy, pedunculotomy, lobotomy, removal of cortical scars etc.

Vesterdal, Foght-Nielsen and Thomsen (1954) studied 214 consecutive P.E.G.'s in a paediatric department. They divided their material according to clinical diagnosis, and found among 30 cases of epilepsy normal lateral ventricles in 23, cortical atrophy in 3, slight dilatation of the lateral ventricles in 4, moderate dilatation in two, and only in one case was there no filling of the ventricular system. In 30 mentally retarded patients 15 had normal lateral ventricles and two of these had in addition cortical atrophy. Dilatation of the ventricular system was slight in 3 cases, moderate in 9 and severe in two. The combination of mental retardation and epilepsy was present in 25 children of whom 8 had a normal ventricular system; 6 had slight dilatation, 6 moderate and 5 severe. When the material was divided according to aetiology 69 patients had perinatal damage. Of these 22 had a normal system, 12 slight dilatation, 25 moderate and 6 severe. Internal porencephaly was found in two cases and no filling of the ventricular system in two cases. Twenty children suffered from postnatal infective damage and here the ventricular system was normal in 7, slightly dilated in 4, moderately in 6 and severely in 3. The remaining 112 children had a variety of aetiological factors. In this group a normal system was present in 52, slight dilatation in 27, moderate in 22 and severe in 5. The authors concluded that the clinical picture, especially of unilateral disorders such as hemiplegia and Jacksonian epilepsy, agreed with the P.E.G. findings.

Like other French authors, *Roulleau et al.* (1957) were very enthusiastic about the use of P.E.G. in almost every possible nervous disorder of childhood. Of 38 patients a group with tuberculous meningitis was of special interest, and it was shown that 5 of them had normal P.E.G.'s and subsequent development was normal.

Hagberg et al. (1959) investigated the risks, indications and technical considerations of P.E.G. in 123 children under 15 years, of whom 35 were under two. Serious complications such as shock during insufflation, cessation of respiration or other serious conditions immediately after P.E.G. were seen in 5 children in the age group below two. No serious complications were seen among the older children. Minor reactions in the form of fever, headache, nausea and, in a few cases, slight meningeal reactions were seen in 12 out of 36 examinations in children below two, and in 27 out of 47 in children over 8. They had no deaths in their series.

Müller (1958a) described the pathogenesis of hydrocephalus with particular reference to physical factors. He emphasised that one could not rely on the size of the ventricular system unless the entire sub-arachnoid space was filled, 70-100 ml., and when could one be sure of this? He could not agree

that a definite conclusion could be reached concerning the pathogenesis of cerebral palsy (as stated by *Brenner*, p. 41 and *Guttmann*, p. 41) or that it should be possible to relate a number of psychiatric disorders such as endogenous psychosis to the P.E.G. findings. Measuring methods, indices and particularly planimetric methods were said to be of little value.

Huber (1958) was very critical of *Müller* and did not think his conclusions were justified. *Huber* was of the opinion that slow insufflation of air through the lumbar route or, as suggested by *Schaltenbrand*, passive intake sub-occipitally, could not alter the size of the ventricular system.

(c) *Reactions to P.E.G. in children.*

In addition to minor reactions mentioned in the various reports, e.g. slight rise in temperature, headache etc., some reports deal with more specific reactions. *Hockerts and Böcking* (1950) found the capillary resistance was increased in children after the examination and was maximal an hour later, becoming normal within four to twenty-four hours. They suggested that this was a neuro-vegetative influence. In an attempt to prevent neuro-vegetative reactions *Bleckmann and Salus* (1955) gave "Megaphen" (a chlorpromazine derivative) to 13 children prior to P.E.G. Nevertheless, two of the treated children developed circulatory collapse but improved immediately when lobeline and peripherin were given. They found no noticeable prophylactic effect with "Megaphen". However, they showed in 7 children over 10 years of age that a combination of "Megaphen" and a sedative had a favourable influence on the patient's course after P.E.G.

As in adults E.C.G. changes were found in children during P.E.G. *Schaper* (1955) found changes in 48 out of 50 patients. All changes were slight and disappeared within two hours.

(d) *Complications and mortality.*

Previously a number of reports have been discussed in which fatalities were recorded. These may be found in Table 1 (p. 26) together with similar information from adult and mixed materials.

With regard to complications *Rupilius* (1934) discussed pathological findings in 200 children. He found 30% had a rise in temperature to more than 38.5°C. Four children had more serious complications, viz. headache, neck stiffness and vomiting. A six-month-old infant with convulsions died and at autopsy death was found to be due to an air embolus. He was the first to emphasise the value of repeated P.E.G.'s, and in a series of 27 cases he found there were some differences, and therefore care had to be taken with evaluation especially of air over the surface of the brain in patients between six and eighteen months of age, and particularly when there is poor ventricular filling. He emphasised the value of comparing abnormal P.E.G.'s

and autopsy results and found in 17 of 20 cases P.E.G. findings were confirmed. *King and Otenasek* (1948) described a child as well as an adult who died from air embolus.

A rare complication was described by *Kerman, Perlstein and Levinson* (1943) viz. a case of pyocyanus meningitis which was believed to have originated in the bottle through which helium had been filtered before insufflation. A similar case was reported by *Iwasaki and Motinaga* (1939).

Charash and Dunning (1956) in a series of P.E.G.'s originating in a State institution for mentally retarded, carried out 181 on 23,509 admissions between 1938-1954. They had two deaths among 106 patients with mental retardation alone, 7 had serious complications and 30 minor complications, and among 45 children with epilepsy two had serious and 11 minor complications. They were critical of other reports which found this examination less dangerous. *Matson* (1957) commenting on the report, pointed out the great quantity of cerebrospinal fluid withdrawn and concluded by emphasising that such results did not discourage his department from using the examination which must be considered to be without danger when performed in the right way. He recommended V.E.G. in children below the age of a year.

(e) *Special findings and considerations.*

The question of the size of the sub-arachnoid space has been discussed already by *Sauer* (1927) who drew attention to the fact that the sub-arachnoid space could not be smaller in children than in adults but that the opposite was the case.

Grävinghoff (1928) supported this point of view especially in infants, and found that below 6 years of age one could not rely on the sub-arachnoid findings. *Saamer* (1934) discussed misinterpretations with changing head positions and showed that the distribution of surface air, especially that occurring unilaterally, could be altered. The problem of sub-dural air findings was discussed by *Boudreau and Crosby* (1958) who in 159 children below two found sub-dural air in 66. Of these 66 patients 60 had operations performed, and in 35 of them with a large amount of sub-dural air 33 had sub-dural effusions or haematomas. In 17 patients where the changes were less pronounced, and where the air collection did not move freely 6 had haematomas or effusions. Operation on 8 patients revealed pathological conditions sub-durally in 4 where it was only a question of small amounts of air around the tentorium or falx. The authors also examined children on whom operations had been performed for sub-dural disorders and in whom no sub-dural air had been seen. In the same period of four years they found 15 patients of whom 12 had had several punctures performed before the insufflation and operation which the authors felt was the explanation of the missing air in the sub-dural space. They found that air could be seen more often in the sub-dural space if this already contained fluid so that the otherwise narrow

space was sufficiently dilated to allow air to enter it. As a consequence of their investigation they recommended that all such children should have an exploratory operation to exclude membranes and/or fluid.

The question of chronic internal hydrocephalus was considered by *Stutte* (1941). In his study of 22 children he emphasised that an increase in head circumference was not necessarily associated with this condition but that a pronounced prominence of the forehead was often seen. Due to pressure on the pituitary gland and the vegetative centres, constitutional dysplasia was frequently found accompanied by disturbance of growth, eye changes (nystagmus, anisochorea, pseudo-neuritis), and in a single case decreased hearing. The children were often retarded, especially in speech. There was no relationship between the I.Q. and degree of dilatation and not less than 12 of the children showed normal intelligence. Eleven of these patients had dilated third ventricles, and only two had increased amounts of sub-arachnoid air.

Although *Ingraham and Matson* (1944), in their classic work on sub-dural haematoma in infancy, stated that P.E.G. was not necessary in such cases where puncture had established the diagnosis, their report showed a good example of the value of P.E.G.

The problem of sub-dural air and sub-dural fluid was discussed by *Smith and Crothers* (1950) and they stated that at least one-third of these findings were due to incorrect positioning of the needle. The younger the child the more frequently sub-dural air was found. Of 37 children below two years of age sub-dural air was found in 27. They investigated the relationship between air and the presence of fluid in the sub-dural space and found that among those children who had complained after the insufflation sub-dural fluid was found more frequently. They thought that this was the result of vessel tears during insufflation so that, in reality, a sub-dural haematoma was produced. The finding of sub-dural effusions following bacterial meningitis was described by *Matson* (1953).

Shapiro and Tosti (1940) described ventricular dilatation in cases of spina bifida but were unaware of the possible presence of Arnold-Chiari's malformation at the time their autopsies were performed. The simultaneous occurrence of microcephaly and ventricular dilatation was described by *McClelland* (1940) who found this combination in 13 of 142 neuro-paediatric patients and he suggested the term "hydromicrocephaly".

The frequency of Kehr's microventriculie was examined by *Schönenberg and Ott* (1953) who found it in 19 of 1026 patients. A similar study was made in 1957 by *Kohler* who found that 34 of 486 patients had microventriculie.

In 1951 *Zellweger* showed that what were believed to be Verga's cysts frequently turned out to be inter-ventricular cisterns. He thought that this phenomenon was connected to a hypoplasia of the callosal body. Forty-five children with malformations of the midline of the cranium were described

by *Thieffry et al.* (1958). In a series of 30 boys and 15 girls they found 12 with absence of the septum pellucidum (single ventricle) and 8 with absence of the callosal body. Fifteen children had inter-ventricular cisterns and 11 cyst formation; of these 5 were in the septum pellucidum and 6 were Verga's cysts. Both *Zellweger* and *Thieffry* found the prognosis was generally poor in these cases. Some information on the incidence of such changes generally can be obtained from a pathological anatomical study by *Schwidde* (1952) who found cysts in the septum pellucidum in 20% of 1032 consecutive brain examinations (69 male and 31 female). Approximately 2% had Verga's cysts but in no case was it an isolated finding.

In recent years a great number of case reports have been published which should be briefly mentioned. *Hamby et al* (1950) performed V.E.G. in 4 of 7 patients with hydranencephaly and found total filling of the cranium with air. *Brandt, Christensen and Vesterdal* reported a case where the P.E.G. could have been interpreted incorrectly because of the amount of surface air (present author's case no. 170, p. 145). The fact that the surface air changed between one examination and another should suggest that this finding is of no significance as it occurs in an age group where changes in the subarachnoid space are unreliable.

Jakab (1954) followed a child with Heller's syndrome and found increased changes in the P.E.G. The necessity for P.E.G. examination before hemispherectomy in children was emphasised by *Ferey et al.* (1954) who obtained excellent results in two cases. *Fausser* (1955) examined a 15-month-old girl with an isosexual pubertas praecox and diffuse cerebral atrophy, and he was in absolute agreement with *Thamdrup* in presuming a cerebral aetiology for the disorder.

A case report of anoxic changes leading to the most serious degree of porencephaly was reported by *Pretorius and Pretorius* (1955).

Three children who sustained brain damage and at the same time clinically resembled patients with myxoedema, were described by *d'Avignon and Zetterström* (1956) but only one child was examined by P.E.G. Absence of the callosal body in 4 cases was discussed by *Foght-Nielsen, Thomsen and Vesterdal* (1954) who considered that the condition was symptomless but was frequently combined with other malformations.

Vinken and Strackee-Kuijer (1957) described two patients with absence of the septum pellucidum and discussed similar findings. They drew particular attention to the fact that clinically such patients often have epilepsy and eye symptoms such as nystagmus, papilloedema and atrophy of the optic nerves.

(f) *P.E.G. and autopsy findings.*

Dannenbaum (1926) emphasised the great value of comparing P.E.G. findings with autopsy findings. Later Rupilius (1934) suggested confirming P.E.G. findings in the same way.

Kruse and Schaetz (1935) in an extensive monograph correlated the autopsy findings and the P.E.G. findings. From a total of 22 case reports they selected 9 which they discussed in detail, and where they found a close correlation. Malamud and Garoutte (1954) reported their findings on 30 patients who died in a State institution for mentally retarded. Twenty of the children were diagnosed as malformations and 7 of them showed no surface air frontally on P.E.G. The group consisting of secondary brain damage was made up of 10 children and these they divided into 4 sub-groups according to the pathological anatomical findings. The dilatation was not of diagnostic help as it was such a common finding.

(g) *P.E.G. in brain-damaged children.*

As already mentioned, studies have been performed on children suffering from epilepsy, cerebral palsy and mental retardation and in various combinations (Vesterdal *et al.*, Wolff).

In 1930 Crothers, Vogt and Eley posed five questions and attempted to answer them with regard to children with "fixed" brain lesions. Their material consisted of 200 patients, all of whom had L.E.G. The questions and answers were as follows:

(i) Q: Is a definite diagnosis possible without it?

A: This must always depend on what is regarded as a definite diagnosis and also on many other factors.

(ii) Q: Is the procedure likely to clarify the situation and to what extent?

A: Yes, in approximately 50%.

(iii) Q: Is there any likelihood that conditions will be made worse?

A: Probably not. On the contrary, it has frequently been found that fewer seizures occur after the examination and reduction of motor or mental capacity has never been seen.

(iv) Q: Is the mortality serious?

A: There was one death among the 200 examined. The child had suffered from a progressive disorder since the age of 6 months. He died without warning just before he was due to be discharged on the 19th day after insufflation and his death appeared to have no direct connection with the examination.

(v) Q: How severe is the reaction?

A: Reactions occur either immediately following the examination or after 24 hours in the form of a meningeal reaction but of no real severity.

The authors fully supported the examination and concluded that care had to be taken in the interpretation of surface air. They stated: "We are, of course, unable and unwilling to make diagnostic or prognostic decisions on the basis of encephalograms alone."

Eley and Vogt (1932) emphasised the value of P.E.G. in the classification of cerebral palsy, oligophrenia and epilepsy in children. In this work they discuss in detail the different reactions which, in their opinion, can be divided into (1) Immediate: sweating, pallor and change in pulse rate due to change in pressure. (2) A similar reaction occurring approximately 30 minutes after insufflation. (3) Approximately twenty-four hours later where a meningeal reaction led to fever, neck stiffness and a positive Kernig's sign.

Crothers et al. (1942) in discussing the prognosis of encephalopathy in children underlined the fact that one must not be satisfied alone with presumed recovery but must make sure that further development proceeds normally. They reported a most interesting case history in a year old girl who had suffered from pneumococcal meningitis and whose P.E.G. showed slight dilatation of the ventricular system. Four weeks later the patient developed a severe hemiplegia and an abscess was drained from the frontal lobe. P.E.G. performed seven years later showed a normal ventricular system with only slight displacement, and the authors felt that there had been a true restitution of tissue in the abscess area.

Salomonsen, Eek and Skatvedt (1957) showed that P.E.G. findings in children with cerebral palsy, oligophrenia and epilepsy were approximately the same as the clinical findings and often overlapped.

(h) *P.E.G. in epilepsy.*

In addition to previously mentioned reports dealing with the findings in epilepsy, the work of *Bamberger and Matthes* (1959) should be mentioned. In a series of 349 children with convulsions they performed P.E.G. in 137 and found 49 with normal ventricular systems; 41 showed symmetrical dilatation, 41 asymmetrical dilatation and 5 malformation. They considered the examination of great value in children with epilepsy.

Skatvedt, Eek and Gardborg (1959) in a series of 165 patients with convulsions found 60% with abnormal P.E.G.'s. The earlier the onset of the disease the more frequent and severe were the changes. They found in children whose convulsions started before two years of age 80% with abnormal P.E.G.'s. There was no definite correlation between the severity of the disease and the P.E.G. pictures, and no relationship between the E.E.G. and the P.E.G. In 40% of the children with abnormal P.E.G.'s the aetiology was unknown but it was presumed that prenatal damage was involved.

(i) *P.E.G. in cerebral palsy.*

Guttmann (1929) studied the value of P.E.G. in cerebral palsied children with hemiplegia. He found three major types of changes: (1) Hemiatrophy, with or without porous formation, as a result of scar formation in the still immature brain of the infant. (2) Sequelae of encephalitis and (3) Developmental malformations.

Crothers lecturing in 1938 on P.E.G. changes in spastic hemiplegics stated that one could either believe it was pressure from one side or a pull from the other, or it could be due to unequal growth of the hemispheres. He emphasised the importance of the growth factor in children and said: "In general, every one believes that this is a procedure of great value in diagnosis and prognosis, but there are a few situations in which gross errors are possible if the factor of growth and development is ignored or underemphasized," and similar viewpoints were again emphasised in 1941 (*Crothers and Wyatt*). A child with a progressive atrophy and motor symptoms was studied by *King* (1938). Repeated P.E.G.'s showed clear progression of the dilatation and the findings were confirmed finally at autopsy.

Brenner (1941, 1942) dealt with the changes in cerebral palsy and in a more extensive paper discussed the general considerations of P.E.G. in childhood. As in previous works, he made an extensive review of the literature to which reference may be made concerning special points outside the scope of this work. He divided P.E.G. findings into nine types and related them to the pathogenesis:

P.E.G. findings

1. Normal.
2. Rounded angles.
3. Cylindrical lateral ventricles.
4. Rectangular to prism-shaped lateral ventricles.
5. Circular third ventricle.
6. Narrow, column-shaped ventricle.
7. Fusion of the lateral ventricles.
8. Displacement of ventricular system.
9. Gross asymmetry of cerebrospinal fluid circulatory system.

Pathogenesis

- Endogenous factors.
 Damage in the first month of foetal life.
 As in (2).
 Birth injury.
- Disturbance of cerebrospinal fluid circulation at an early stage but now restored.
 Malformation (he interpreted this as agenesis of the callosal body).
 Malformation (agenesis of septum pellucidum etc.).
 Meningopathic or meningoencephalitic processes remote from ventricle.
 A number of different causes, e. g. porous formation and congenital malformations etc.

In a survey of diagnostic procedures in cerebral palsy, *Perlstein and Barnett* (1952) stated that the patient should have a complete investigation including X-rays of skull and long bones, full blood examination, eye examination and possibly sub-dural puncture. If the patient was more than

three months old, E.E.G. should be performed. P.E.G. should be undertaken in selected cases and concerning this selection the authors state: "Correlations between clinical and pneumoencephalographic findings are not too great. However, it is of value in corroborating a diagnosis of sub-dural hematoma, marked cortical atrophy, neoplasms, internal hydrocephalus, and certain anomalies of the brain."

Andersen (1954, 1957) found among 186 Norwegian patients with cerebral palsy that P.E.G. was performed in 20 and concluded that this examination was of no special value in this disease. He found a close correlation between P.E.G. and E.E.G. except for three cases with cortical atrophy of which only one had an abnormal E.E.G.

In a series of 320 patients with cerebral palsy *Eek* (1955) performed P.E.G. in 85 of which 27 were unsuccessful. In the remaining 58 he found 48 with pathological changes of which 47 were of the central type.

Denhoff et al. (1956) used P.E.G. for prognosis in 50 cases of cerebral palsy which were divided into 7 sub-groups.

From Italy came a report of 67 P.E.G.'s performed on patients with cerebral palsy by *Battisti et al.* (1958). *Skatvedt* (1958) in her monograph on cerebral palsy reported 105 P.E.G.'s in a series of 370 patients. These examinations were evaluated by *Eek* who found 84% of the P.E.G.'s were abnormal, the greatest number occurring in the group with mixed types of cerebral palsy and tetraplegia and the smallest in the groups of ataxias and athetoses. The most reliable information was obtained in cases of hemiplegia.

In *Crothers'* last publication (*Crothers and Paine* 1959) he said that much information could be obtained by P.E.G. and gave two major indications for the examination: (1) Cases where an active process could not be excluded and (2) Unilateral severe seizures. Apart from these indications the authors used the examination less and less but stated that it should be left to the examiner in each individual case to decide how important it was to know the size of the lesion. One of the reasons for the increased reservation was the risk of sub-dural effusions, especially in infants, a point *Crothers* had made at an earlier time. Information regarding prognosis was seldom more definite even if P.E.G. had been carried out. They found a relationship between the degree of dilatation and intellectual development in patients with hemiplegia, the only clinical group thus evaluated, but they also found the opposite illustrated by a patient who had a severely dilated system but a normal I.Q.

(j) *P.E.G. and mental retardation.*

Opinions on the value of P.E.G. in mental retardation have been divided. As previously stated, *Casamajor, Laidlaw and Kozinn*, in their series of 500 children, found P.E.G. of no practical value. *Levinson* (1947) examined 800 mentally retarded children and had no immediate mortality, but two children died 2-3 days after insufflation. He found a number of compli-

cations, e.g. slow pulse and respiration rate, fever, headache, restlessness and in a few cases pneumonia and meningitis (3 patients). He stated that localised cortical atrophy had a fairly good prognosis and generalised cortical atrophy a hopeless prognosis. As regards the latter he stated: "Cases of this type have no future at all and must be institutionalized. The same is true of porencephaly." The lack of sub-arachnoid air, especially on one side, was indicative of arachnoiditis. Ventricular dilatation was seen in all cases of cortical atrophy and displacement of the ventricles most often meant a tumour or an abscess.

The therapeutic use of P.E.G. in children with mental retardation was reported by *Miller and Delage* (1950). It was not only the effect of the insufflation but also possibly the effect of an intrathecal injection of 25 mg of vitamin B₁ which they gave at the end of the examination. Even if it was impossible to demonstrate an improvement in I.Q., they were of the opinion that the less severely retarded children became more alert.

A report by *Charash and Dunning* (1956) on 106 mentally retarded patients has been discussed previously because of the high incidence of complications, p. 36.

Gillet et al. (1957) examined 95 children over 5 years of age and found no difference in the number of normal P.E.G.'s in a group of children with an I.Q. below 50 and a group with an I.Q. above 50. Mental retardation accompanied by convulsions showed a ratio 10/13 of normal and abnormal P.E.G.'s in contrast to mental retardation without convulsions where the ratio was 14/29. They had no deaths in their series and only the usual complications.

An attempt to relate P.E.G. findings to the child's behaviour as measured by Gesell's test and by other psycho-neurological tests was performed by *Knobloch et al.* (1958). The different examinations were carried out independently of one another and were compared later. They found no correlation between P.E.G. and adaptive developmental quotients whereas if gross motor developmental quotients were used it would seem that the lowest values were associated with the more severe P.E.G. changes. The authors conclude: "One is not justified in making a diagnosis of mental retardation on the basis of the pneumoencephalogram."

(k) *P.E.G. and prognostic considerations.*

In 1930 *Crothers, Vogt and Eley*, as quoted earlier in this chapter, said: "We are, of course, unable and unwilling to make diagnostic or prognostic decisions on the basis of encephalogram alone." This was followed by a study in the same centre by *Brines and Lord* (1939) who concluded that care must be taken when assessing the pictures. They gave some examples all of which with the exception of case no. 1 could be placed in the moderate atrophy group, if measured by the method used in the present work.

Amatruda (1942) in Gesell's clinic examined 53 children with cerebral pathology in order to evaluate the prognostic significance of P.E.G. and found that one could not attach any importance to it. Of the 53 patients, 11 developed normally in spite of definite X-ray findings of cortical atrophy. Of these patients one was in the group of post-meningitis conditions, two in the communicating hydrocephalus groups and 8 were in the group of epileptics. She states: "It does not picture the functional capacity of the cerebrum except when this capacity can be inferred from structural defects, such as tumors, obstructions, and porencephalies. The presence of dilatation of the ventricles and of widened cerebral sulci, or so-called cortical atrophy, does not necessarily indicate any alteration in cerebral function or any diminution in its developmental potentialities," and further "In the presence of normal behavior, pneumoencephalographic evidence of cortical atrophy, so-called, is prognostically meaningless, because behavior is the final criterion of the functional integrity of the central nervous system." Reviewing these 11 patients, one finds that in the case of one patient (D.6) in the group of communicating hydrocephalus, no conclusion can be drawn because there was no ventricular filling and the diagnosis of hydrocephalus in this case was based on an increased head circumference and an impression of thin cranial bones. In the second case (D.7) the ventricular dilatation was borderline and, therefore, arrested hydrocephalus could have been the explanation. The patient in the post-meningitis group was 25 months old when dilatation of the ventricular system and bilateral cortical atrophy was found. A short time before the examination the patient developed an acute disorder and was treated with sulphonamides. He had neck stiffness and vomiting and was at the time of examination slowly recovering. His developmental score then corresponded to 21-24 months. At follow-up five months later the score corresponded to 33 months. Such a case history does not mean very much because the initial examination was carried out at a time when the patient had only just recovered from the acute disorder. The follow-up five months later revealed that the patient was normal and above average development but we do not know his intellectual score before the illness. In her final group of 8 patients patient no. 7 was not followed up and was at the original examination an imbecile. Patient no. 8 with dilatation of the ventricular system and minimal cortical atrophy on the right side was slightly retarded at the time of P.E.G. and at follow-up at 7 years of age his I.Q. corresponded to 18 months. In this case it is impossible to say that there had been "a normal development in spite of encephalography." Three of her cases examined at 13, 15 and 16 months respectively were said to have bilateral cortical atrophy and the X-rays of two of them showed normal ventricular systems. With regard to the conclusion one might be permitted to disagree with the author and say that P.E.G. is of definite prognostic value.

Vigouroux et al. (1954) studied the value of P.E.G., angiography and

E.E.G. in 100 children with "encephalopathia infantilis." The P.E.G. was normal in 29, diffuse changes were found in 38 and localised changes in 33. The older the children were the more normal the findings. E.E.G. was abnormal in 94 cases (41 diffuse changes, 53 localised). The authors were certain of the prognostic value of P.E.G. and stated that the more serious the changes were the worse the prognosis but they did not enlarge on this statement.

In *Anderson's* study of 400 children (1951) he found it was a relatively simple and safe procedure of considerable value. He followed 19 children after the examination and found that 9 of the children with abnormal P.E.G.'s had done well and showed clinical improvement. (One was examined immediately after the acute phase of meningitis and another showed an increased amount of surface air when 4½ months old). Eight patients were mentally retarded but had normal P.E.G.'s. At autopsy one of the 8 was found to be suffering from Tay-Sachs' disease and another from Schilder's leucoencephalopathy. In this series there were 6 deaths, one during the examination and the remainder one to five days afterwards.

Before concluding this section it is of interest to note that some of the latest reports on X-ray examinations in diseases of the central nervous system in childhood deal with angiographic findings. It is said that this examination is not usually dangerous even in infants and frequently gives excellent results especially in cases of sub-dural haematoma and tumour (*Forlani and Wiedemann* 1960). In many cases the angiogram adds little to the P.E.G. findings and is frequently inferior to the P.E.G. It should be emphasised that the examinations may be supplementary to one another in a great number of cases, (*Claus and Heidrich* 1960, *Meyer and Busch* 1960).

As can be seen from the paediatric point of view there has been a considerable interest in P.E.G. which has uncovered a vast store of information. It is however rather disappointing to see how little attention has been paid to this type of examination, its risks and value in neuro-paediatric textbooks. As a rule results are only available as illustrations to case histories. (*Ingraham and Matson* 1954, *Dekaban* 1959, *Jackson and Thompson* 1959, *Ford* 1960).

C: THE DEVELOPMENT OF PNEUMOENCEPHALOGRAPHY IN DENMARK

The first time P.E.G. was reported in Denmark was at a Danish Neurological Society meeting in November 1922 when *Schrøder* presented a case history of a 28-year-old male patient with convulsions who had had Dandy's insufflation performed in the Municipal Hospital's surgical department V for a suspected cerebral tumour. He was admitted on 19th August, 1922, and on the 28th there is a note to the effect that it was intended to inject air into the right lateral ventricle according to Dandy's method. It was unsuccessful and after several attempts the procedure was abandoned. On 31st August a

puncture was made on the left side but was unsuccessful. Following this lumbar puncture was performed with difficulty. 24 ml. of fluid were withdrawn and were replaced by air filtered through cotton. X-ray report described the air filling the ventricles with little air on the surface. The left lateral ventricle was somewhat smaller than the right but of a normal shape. It could have been due to diffuse atrophy as no isolated or localised tumour was found. (Signed G. Biering). Following the examination the patient developed a headache and a rise in temperature ($38^{\circ}\text{C}.$). On the 7th September a trephine was performed and showed normal conditions on the left side. This first insufflation was performed by the head of the department Professor P. N. Hansen.

In the following years there was no reference to this examination whereas a number of reports of contrast (lipoidol) studies were mentioned. Two large reports on the diagnosis of brain tumours (*Wimmer* 1923, *Christiansen* 1929) do not mention P.E.G. at all. In 1930 *Jessen* in Århus lectured on "external" tumour diagnosis in the central nervous system, and in 1932 at the Medical Society in Copenhagen on the diagnosis of neurosurgical cranio-spinal disorders (published 1933a). This was the first Danish survey of P.E.G. At the meeting in Copenhagen the discussion was interesting. Some rejected this new method (*Christiansen*) and others supported it but suggested that it might be a dangerous procedure adding, however, that cerebral tumour was a dangerous condition, (*Krabbe*). There was a strong feeling that a new speciality, namely neurosurgery, should be created (*Fenger*).

Dahl-Iversen who was one of the P.E.G. pioneers in this country recorded his experiences and results in 1933, and gave an excellent review of indications, contra-indications and complications.

Jessen (1933b) reported favourable therapeutic results of P.E.G. in headache and this was followed by another publication from the same clinic by *Roepstorff* (1939). In a series of 284 patients he found that only 96 were afebrile following the examination. The fever was generally of short duration and was not marked. A similar finding was recorded by *Dahl-Iversen*.

In 1944 *Busch* reported a new method of sub-occipital encephalography on anaesthetised patients lying in the horizontal position. He compared the results with L.E.G. where no ventricular filling took place in 8–15% and where the rate of complications, headache, vomiting, dizziness etc. was rather high with the results obtained by S.E.G. using the new method. Complaints were few when this method was employed and the lack of filling was similar to L.E.G. (14 out of 153 examined).

Magnussen (1950) studied psychiatric patients using L.E.G. and S.E.G. alternately. In 21 months 178 P.E.G.'s were performed (81 L.E.G.'s and 97 S.E.G.'s of which 13 also had L.E.G.'s). *Magnussen* found with L.E.G. there was a lack of filling of the ventricular system in two out of 80 patients whereas with S.E.G. there was lack of filling in 22 out of 96 patients.

There was one death after S.E.G. Headache following the examination was approximately 12 hours shorter in duration than with L.E.G. He summarised the advantages as follows: the position is suitable using Busch's head support. There is no collapse and few complaints. The disadvantages are lack of filling in approximately 20% and a possible risk of complications. The advantages of L.E.G. are less frequent lack of filling and a very small risk involved. The disadvantage is more complaints. His conclusion was that in non-specialised departments L.E.G. should be the routine method used because of the aforementioned advantages.

Following the 11th Scandinavian Congress of Neurology in Copenhagen in 1950 a number of papers on P.E.G. were published in 1951. *Simonsen* reported unilateral cerebral ventricular dilatation in cryptogenic epilepsy. Of 338 examinations a normal ventricular system was found in 223, diffuse symmetrical dilatation in 65, unilateral ventricular dilatation in 95 of which 70% occurred on the left side. He drew attention to the fact that this rate corresponded to the rate of the first head position at birth as compared to the second head position. He suggested that a unilateral cerebral anoxia had been present at birth but had not been recognised.

Trolle and Fog studied 500 consecutive P.E.G.'s in non-surgical neurological patients. They used the following terminology: slight, moderate and severe ventricular dilatation, diffuse and localised cortical atrophy. Of these patients 116 were less than fifteen years old and 60% were males. The diagnosis was unchanged after air study in 337 patients, was definitely established in 46 and amended in 95. P.E.G. was unsatisfactory in 22 patients. In a survey of epileptic patients they found that in cases of cryptogenic epilepsy atrophy was present in 16% and in symptomatic epilepsy in 95%. The authors concluded: "This study supports the view that the indications for encephalography should be enlarged rather than restricted. The method should be applied not only in epileptic patients and in cases where an intracranial tumour is suspected. It may also add considerably to diagnosis in post-concussional syndromes and cases of cryptogenic headache."

Wagner favours the examination in patients with personality changes appearing late in life. He studied 277 such patients by P.E.G. and found probable atrophy in 85 cases, definite changes in 66 and doubtful changes in 19.

Henrichsen presented at the Congress a survey of P.E.G.'s in 300 mentally retarded patients. Unfortunately his material has not been published and it has not been possible to obtain further information.

The results of P.E.G. in patients from the paediatric department were published in 1954 by *Vesterdal, Foght-Nielsen and Thomsen* and this is discussed on p. 34.

Hertz and Strandberg (1954) compared the results of treatment in two groups of patients with post-concussional headache, one treated by Silfver-

skiöld's method and the other by P.E.G. They found that Silfverskiöld's method was superior especially if the condition had been present for a short time in younger patients. P.E.G. in the 38 examined was abnormal in all.

Jacobsen (1955) studied the KZ-syndrome (sequelae of concentration camp imprisonment) with P.E.G. and found 8 out of 12 had definite atrophy, one had doubtful changes and 3 were normal.

Brandt et al. (1955) recorded their experiences with children with special emphasis on the technical aspects of L.E.G. The reactions which occurred e.g. fever, headache etc. they considered unimportant.

Hammerberg and Fog (1959) studied the clinical value of X-ray diagnosis of cerebral atrophy. During a five year period 602 P.E.G.'s were performed on adult neurological patients of which 332 were abnormal. Compared with the normal group of 270 there was an almost uniform distribution with regard to neurological diagnosis but there was an increase of vascular disorders in the group with ventricular dilatation. The average in the group showing changes was 46.3 years as compared with 32.4 years in the normal group. In cases showing impaired intellectual performance or dementia, there was possibly a correlation between X-ray diagnosis and the clinical findings. There was no correlation between E.E.G. and increased ventricular volume.

In addition to these reports of gross findings, there have been reports of factors which are relevant to the present work. *Riskær* (1944) discussed cysts and tumours of the septum pellucidum, and emphasised the value of P.E.G. in diagnosis. *Foght-Nielsen, Vesterdal and Thomsen* (1954) discussed the absence of the callosal body in four cases. *Thamdrup* (1955) emphasised in 17 children with precocious puberty that 12 had serious cerebral disorders and of these 8 were studied by P.E.G. and the changes found involved the hypothalamic area.

Bertelsen (1958) in his monograph on premature cranial synostosis reported P.E.G. findings in 48 cases out of a total of 219 studied. He found in 9 patients between birth and 9 years that 7 had slight dilatation of the ventricular system, and in 10 patients between 11 and 20 years one had slight dilatation and 3 moderate dilatation.

To celebrate the 25th Anniversary of the Neurosurgical Department in 1959 a number of reviews of the results obtained in different fields of neurosurgery were published, and among these was a review of the present state of neuro-radiology by *Jacobsen*.

D: METHODS OF MEASURING PNEUMOENCEPHALOGRAMS

There were a great number of reports of measurements made on P.E.G.'s because for many years it was hoped that the size of the ventricular system could be recorded accurately thus avoiding such general terms as slight,

moderate or severe dilatation of the ventricular system. The methods fall into two major groups:

- (a) Planimetric measurements.
- (b) Linear measurements.

A third group (c) of measurements of the ventricular system at autopsy will be discussed as this provides an opportunity for direct measurement and avoids errors due to technical difficulties associated with the X-ray examination.

(a): *planimetry* was first used by *Abramowitsch and Winkler* (1930). They used measurements on the anterior-posterior projection as well as the lateral projection and by measuring different distances calculated the area. The method was inconvenient and cannot be employed in daily clinical practice. Some of the distances measured were very small and could easily lead to errors in calculation. Furthermore, they used different lines which were not easily defined, e.g. a line drawn at right angles to the mid-point of a line from glabella to inion, and where this line intersected the ventricle one of the figures used in the calculation was obtained.

The exact size of the third ventricle was reported as varying from 2.5-17 mm. in imbeciles and epileptic patients.

In 1939 *Heinrich* published a paper on the normal encephalograms at different ages. He showed that the ventricular system was relatively small in children under six years of age. After this time it increased in size and from the age of ten until approximately 60-65 years it was almost unchanged compared with the cranial area. However, the number of patients studied was small, e.g. in the group below ten years of age there were only 9 children. *Heinrich* found the left ventricle was larger than the right in a ratio of 2:1.

Wolff and Brinkmann (1940) reported a similar investigation. They studied 37 "normal" P.E.G.'s out of a total of 966. They confirmed *Heinrich's* findings that the ventricular system increases with an increase in age. They found the left side was larger than the right in a ratio 2:1. The quotient was calculated from the cranial area on the AP picture and the combined areas of the right and left lateral ventricles. This quotient was for the youngest patient in the material, a girl of 13 years, 50.8 and for the oldest, a 53-year-old man, 19.5.

Planimetric measurements were used by *Kehrer* (1948) who found that the normal ratio between cranial area and lateral ventricle should be between 22 and 30. A ratio between 30 and 40 is borderline and above 40 he called "microventriculie," a condition to which he has given his name. A planimetric calculation of the ratio between the area of lateral ventricles and the area of the third ventricle was performed by *Schiffer* (1951) who found that it was of particular value to measure the third ventricle, especially in the constitutional disease described by *Kretschmer* as puberal dystrophy. If the

ratio was below 6 a marked dilatation of the third ventricle was present.

Rennert (1952) discussed the theoretical basis of planimetric measurements and found that there were a great many possible sources of error e.g. manipulation of the head and bending the head in the sagittal plane could alter the distribution of insufflated air and planimetric measurement was subject to many errors of calculation. He discussed the errors and found it was equally justifiable to use linear measurements, in this instance the width of the anterior horns as compared to the internal cranial diameter. In a report of planimetric examinations in cases of hydrocephalus, *Heidrich* (1955) studied 170 patients, presumably adults, who had a post-traumatic pathogenesis. He used a fixed X-ray focus distance of 90 cm., and reported exact figures of the ventricular size (normal 1.7-2.0 cm) as well as a quotient obtained by dividing the cranial area by the combined areas of the lateral ventricles. Using *Kehrer's* classification *Heidrich's* material consisted of 52 hydrocephalic ventricular systems whereas he found 143. For this reason he introduced another classification as he found that *Kehrer's* limits were too narrow. He stated that a dilated system corresponded to quotients between 11.6 and 42.2, a normal system between 35.0 and 54.3 and microventriculie 46.6 and above. This classification gave the impression of an overlap of the different values as the difference between the smallest degree of dilatation and the largest degree of microventriculie was very small. It should be remembered that *Heidrich* stated that linear measurements such as *Schiersmann's* index only gave a correct result of hydrocephalus in 91 out of 143 patients, and he did not find the index as useful as *Kehrer's* planimetric method. The reader must presume that *Heidrich* already favoured planimetric measurements.

With regard to the third ventricle which was filled in 139 cases, he found it was dilated in 116 and the mean value was 7.8 mm.

Of special interest was the use of the quotient to assess repeated P.E.G.'s. This was done in four cases and showed a good correlation with the clinical course.

Müller (1958a, b) criticised all measurements, especially those which involved minute calculations. He discussed many possible errors e.g. the degree of filling of the system, the distance from the X-ray apparatus, position of the head, the relative distribution of the cranial shape and size and the shape and size of the ventricular system, and gave a number of examples. His criticisms applied to planimetric as well as linear measurements, and he particularly criticised evaluations of side differences where these were found to vary on the different pictures. He emphasised that it was difficult to make any evaluation in childhood.

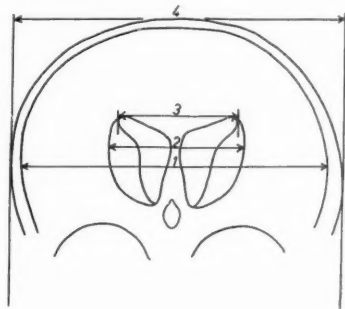
(b): *Linear measurements* fall mainly into two groups:

- (i) Measurements in relation to other measurements giving rise to a ratio or index.
- (ii) Exact figures for the individual ventricular areas.

(i): *Bollea* (1941) measured the ratio between cranial width and the width of the anterior horns on the same line. The ventricular quotient was between 4-4.7 in the normal.

In 1942 two measuring methods appeared simultaneously in the United States and Germany, and have since been most generally used. *Evans* used the greatest width of the anterior horns on AP projection in relation to the greatest internal cranial diameter: width of anterior horns/internal cranial diameter = ratio (Fig. 1). He found among 53 "normal" children that variation of the width of the anterior horns was 2.5-4.4 cm. and variation of the internal cranial diameter 12.8-16.4. The ratio for a small cranium was 0.261 and for a large cranium 0.265. The calculation showed that the standard deviation of the ratio was 0.04 whereas the deviation of the anterior horns was 0.44 and this led *Evans* to believe that the ratio was a better measurement than the exact figure. He studied the ratio in 159 patients with ventricular dilatation

Fig. 1.
Case No. 138.



- | | |
|---|------------------------------|
| 1: INTERNAL TRANSVERSE DIAMETER OF THE SKULL | } EVANS' MEASUREMENTS |
| 2: TRANSVERSE DIAMETER OF THE ANTERIOR HORNS | |
| 3: LARGEST DISTANCE BETWEEN MOST LATERAL CONTOURS OF THE CEREBRAL HEMISPHERES | } SCHIERSMANN'S MEASUREMENTS |
| 4: MAXIMUM EXTERNAL TRANSVERSE BREADTH OF THE SKULL | |

and drew attention to the fact that it was necessary to make special reference to surface air, malformations etc., because the ratio gave no information of this. He reported a case of a boy with a progressive brain lesion in whom repeated P.E.G.'s showed an increasing ratio corresponding to clinical deterioration. He found the normal values for the ratio were 0.20-0.24, early or questionable dilatations were 0.25-0.29 and definite dilatations were 0.30 or above.

In a further report in the same year he examined the degree to which a small alteration in the head position influenced the ratio and found that it made little or no difference to the ratio. He administered 50% glucose saline intravenously to some patients immediately after P.E.G. and this had almost no effect on the ratio. In 6 patients he withdrew as much cerebrospinal fluid as possible and found no change in the size of the ventricular system. Examination three and twenty-four hours after the original examination showed slight changes in the ratio of the order of 0.01-0.02. A few children showed changes in the X-rays twenty-four hours after insufflation and these *Evans* felt were against a "fixed" lesion. He examined a number of patients by repeated P.E.G.'s at intervals of a few days and in one case at more than a year's interval, and found a correlation between increasing dilatation and decreasing well-being of the patient.

The index published by *Schiersmann* closely resembled *Evans*' ratio. The index is obtained by dividing the greatest external cranial diameter by the greatest width of the cella media (Fig. 1). Values below 3.0 indicated hydrocephalus, 3.0-3.5 moderate ventricular dilatation, 3.5-4.0 a normal ventricular system and 4.0 and above excluded dilatation. He found the normal third ventricle did not exceed 5 mm. in width.

Göllnitz (1951, 1954) used a ratio which was similar to *Evans*' ratio. The greatest width of the anterior horn and the distance to the internal cranial wall was measured on each side from a line drawn through the falx, septum pellucidum and septum nasi. He stated that this was done on the basis of *Davidoff* and *Dyke*'s measurement but this cannot be so because they measured the greatest width of the cella media and not the greatest width of the anterior horns. *Göllnitz*'s figures correspond closely to *Evans*' ratio:

- < 0.20: microventriculie
- 0.20-0.25: small normal ventricles
- 0.25-0.30: normal system
- 0.30-0.32: borderline case
- > 0.32: dilated system.

but the dividing line is not so well-defined as in *Evans*'. *Göllnitz* found 5 mm. was the maximum width of a normal third ventricle. All his patients were children from a psychiatric department and no gross displacements of

the ventricular system were found, whereas in some cases asymmetry of the lateral ventricles was found, and in these he considered a difference in the ratio of not more than 0.04 to be normal.

In his last paper single measurements were recorded and from these one can obtain the width of the third ventricle in different age groups.

4 yrs. old (2 pts.):	3 mm.
5 yrs. old (2 pts.):	4 mm.
6 yrs. old (6 pts.):	6 mm.
7 yrs. old (23 pts.):	5 mm.
8 yrs. old (33 pts.):	6 mm.
9 yrs. old (30 pts.):	6 mm.
10 yrs. old (36 pts.):	6 mm.
11 yrs. old (40 pts.):	5 mm.
12 yrs. old (27 pts.):	5 mm.
13 yrs. old (22 pts.):	5 mm.
14 yrs. old (22 pts.):	6 mm.
15 yrs. old (15 pts.):	5 mm.
16 yrs. old (18 pts.):	6 mm.

Evans' ratio was used by *Orley* (1952) in his neuroradiological textbook. He used a specially designed ruler which gave the ratio easily. *Cavalieri* (1957) made use of this ratio in an investigation of the ventricular system in mongoloid children. In a series of 16 cases ratios were between 0.20 and 0.27. Davidoff and Dyke's measurements were all within normal limits.

A number of German and Dutch authors used Schiersmann's index. *Brenner* (1952) found that infants under two years of age had a relatively larger ventricular system than older children but still within normal limits.

Schönenberg and Ott (1953) and *Kohler* (1957) examined children with Kehr's microventriculie using Schiersmann's index. The former in a series of 1026 children below 14 years of age found 19 (1.84%) had an index of 6.55-4.02, and that these patients most often belonged to the group with genuine epilepsy. Kohler in a series of 486 children found 88 had an index above 4.0. However, only 24 (6%) children had microventriculie. Exact measurement was only possible in 400 and the condition could only be diagnosed when the index was above 4.5.

Bronisch (1951, 1952) measured the ventricular quotients and found that in a series of 1594 P.E.G.'s 72 had microventriculie according to Kehr's interpretation (4.5%).

Nürnberg and Schaltenbrand (1955) made careful examinations and measurements in a series of 42 "normal" P.E.G.'s. They made a normogram of the width of the cella media as the abscissa and the cranial diameter as ordinate, (unfortunately they did not state whether it was internal or exter-

nal measurements), and from these figures they formed an index which corresponded closely to Schiersmann's methods.

In addition to the above they reported the relationship between the cranial diameter and the width of the third ventricle for which they found the following values:

<i>Cranial width in cm.</i>	<i>Width of third ventricle in mm.</i>
12.3	3
13.0-13.9	4
14.0-14.9	4.6
15.0-15.9	5.3
16.0-16.4	6

In 1958 *Vinken, Rodenboog and Huizinga* published their results for the ventricular index in patients with epilepsy. They included only those P.E.G.'s which were symmetrical. In a series of 539 patients, 89 were under ten years and 191 between ten and twenty years. They used Schiersmann's index because they found it was easier to measure the external cranial width and the length of the cella media than to measure other distances. Boys in the lowest age groups had a ventricular index of 3.92 and girls 3.94. For the higher age groups the index for boys was 4.13 and for girls 4.29. They concluded that values below 3.5 showed definite dilatation in adults and below 3.25 in children.

Vinken and Strackee (1960) continued their investigations of the relationship between the width of the ventricular system and the cranial diameter. They found the width of the ventricular system did not change much with age so they preferred to use exact figures and not an index because the cranial diameter increases, especially in the early years of life. The reports did not include patients under two years of age and in the age group under six years they had only 36 children. By excluding evaluation in the first two years of life where the great changes in the width of the cranial diameter are found, one is already nearing the age group in which it can be considered less important whether one produces exact figures or relative values. The authors stated that the great advantage of using the index was that the distance from the patient and the X-ray apparatus or the film could be ignored.

Krischek (1959) modified Schiersmann's index as a result of his experience of P.E.G.'s in 268 males with epilepsy.

- Index > 4.0: normal system.
- 3.9-4.0: shape of ventricular angles is the decisive factor.
- 3.5-3.9: slight hydrocephalus.
- 3.1-3.4: moderate hydrocephalus.
- ≤ 3.0: severe hydrocephalus.

Ten patients had P.E.G.'s performed on two occasions and the index remained unchanged in all cases. The interval between P.E.G.'s varied from one year and nine months to fifteen years.

Bruijn (1959) preferred to use *Schiersmann's* index because he found the measuring points were easier to obtain than those suggested by *Evans*. He made an extensive study of P.E.G. in the diagnosis of cerebral atrophy. The survey of the literature was most comprehensive but the survey of his own material was less so. The material consisted of 354 patients (211 males and 143 females) who had been admitted to a neurological department in Utrecht in the years 1945-1957 with the diagnosis "cerebral atrophy," a diagnosis made by the neuroradiologist. However it is not possible to obtain information of the age distribution in the material. *Bruijn* insisted on 12 measurements on each P.E.G. and this was only possible in 163 patients. He found a straight-line correlation between the width of the cella media and the size of the ventricular system, but insufficient correlation between the external cranial diameter and the cella distance to be of practical use. Correlation was found between the width of the third ventricle and the cella media in more than 75%. In patients over 20 years of age the ventricular system was larger than in younger patients.

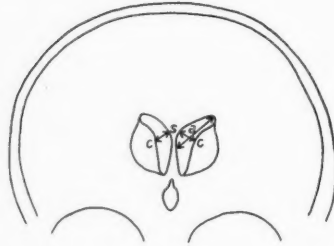
An attempt was made by *Schnitker and Ulrich* (1958) to assess sub-dural air by measuring areas on the right and left side as compared to the capacity of the cranium. They stated that no conclusion could be drawn from the results. They used twenty-four hour pictures and found sub-dural air in 90% of the 66 patients examined.

(ii): Exact measurements indicating the size of the ventricular system are not of the same value in children as in adults because of growth factors in childhood, especially in the first few years. It is possible to use exact values in older children when standard conditions for X-ray examinations are employed.

Larsby and Lindgren (1940) showed in their report on 125 males between thirteen and sixty-one years of age with epilepsy that the lateral ventricles had to be at least 23 mm. to be considered normal, and that anything above 25 mm. was abnormal. This is a narrow margin which corresponds to *Davidoff and Dyke's* figures. They showed that the normal distance between the lateral angles of the ventricular body vary between 3.5 and 4.5 cm. and they stated that values above this indicated a dilated ventricular system. The size of the third ventricle should be 2-8 mm.

Robertson and Childe (1940) gave a number of exact figures for displacement of the ventricular system. They found in a control group of 17 patients who had been examined by operation and where minimal or no lesions were found, that the septum pellucidum and third ventricle were not displaced more than one mm. in relation to the midline, and found mean values of 0.5 mm. In patients with adhesions and without atrophic lesions

Fig. 2.
Case No. 38.



s-c: THE DISTANCE FROM THE SUPERIOR MEDIAL ANGLE OF THE LATERAL VENTRICLE TO THE MOST PROMINENT CONTOUR OF NUCLEUS CAUDATUS. (TROLAND, BAXTER AND SCHATZKI).

a DAVIES AND FALCONER'S DISTANCE.

they found slight displacement of the septum pellucidum (0.3 mm. in 6 patients) but no displacement of the third ventricle, whereas atrophy with or without adhesions showed values of 2.7-2.9 mm. Displacements were most pronounced in patients where the disease was recognised early.

Measurement of the diagonal diameter of the lateral ventricle (Fig. 2) was employed by *Davies and Falconer* (1943) in adult patients. They found that this figure was arbitrary but reliable. It varied in a group of presumed normal lateral ventricles between 15 and 22 mm.

Troland, Baxter and Schatzki (1946, 1947) studied the distance between the upper medial angle of the ventricular system and the most prominent part of the caudate nuclei (Fig. 2). A distance below 1.2 cm. was considered normal, between 1.2-1.4 cm. probably normal, 1.5 cm. borderline and above this definitely abnormal. They used this method for examining changes in the P.E.G. twenty-four hours after insufflation, and found among 60 patients examined that the ventricular system was a little larger on the second day than on the first. They investigated whether a change in the position of the X-ray apparatus influenced the measurements, and found that even a ten degree change hardly influenced the figures.

Durand and Scagliotti (1951) gave exact figures for the ventricular system in children. They found the greatest distance between the lateral angles of the ventricular system was 2-2.8 cm. in infants under 3 months and 2.6-3.4 cm. in infants between 3-12 months. In the second year of life the distance was 3.4-3.8 cm. The width of the third ventricle for the same

age groups was 2-3 mm., 3 mm. and 3-4 mm. Unfortunately it is not possible to discover how many patients were examined in each age group.

Reitmann (1951) measured the ventricular system in 24 patients between 21 and 58 years of age, and found the width of the right lateral ventricle was 20.37 mm. and the left 22.92 mm. The mean ventricular width in males was 23.10 mm. and in females 19.7 mm. He divided the material into two age groups, above and below 40 years of age and stated that no significant change was to be seen in the variation of the ventricular size with increasing age. It may be said that this paper was based on too few patients and the conclusions drawn from it must be viewed with reserve.

Recently several papers have come from Norway concerning measurements on P.E.G's. *Lönnum and Engeset* (1957) used a distance from the upper end of the septum pellucidum to the medial convex contour of the caudate nucleus (SC-distance) and found among 50 patients with a clinical diagnosis of cerebral atrophy that only 6 were below 1.5 cm. and that with increasing distance the patients were worse. As regards the width of the third ventricle *Engeset and Lönnum* (1958) found that values above 12 mm. were associated with an inability to work and had to be considered a most serious finding. Engeset's measurement of the SC-distance was applied to psychiatric patients and was shown to be of great value (*Laane et al.* 1957).

Salomonsen, Eek and Skatvedt (1957) gave a number of requirements for normal P.E.G's. These requirements are the same in later reports by *Skatvedt* (1958) and by *Skatvedt, Eek and Gardborg* (1959) and as stated by *Eek* are: "The ventricular system should be symmetrical, third and fourth ventricle situated in the midline. The two lateral ventricles should be of equal size and found at the same distance from the mid-line on the two sides. The upper lateral corner of cella media of the lateral ventricles should be acute-angled. The distance of the caudate nucleus contour from septum pellucidum (the mid-line) should in anterior view be the same on both sides, and have the characteristic S-shape. A difference in the distance over 2 mm. from the mid-line on the two sides is considered pathological. Maximal anterior width of third ventricle is considered normal in children when measuring under 6 mm. A width of 6-8 mm. is suspect of pathologic dilatation, and when over 8 mm. it is definitely pathological. With a distance over 18 mm. from floor to fastigium in the fourth ventricle it is considered dilated. Maximal width of the two temporal horns in anterior view should not exceed a couple of millimetres. With a width over 5 mm. it is highly suspect of pathologic dilatation. On a difference in the width of the temporal horns over 2 mm. in the same projection, the wider one is considered pathological. The conditions of the basal cisterns and sulci are not estimable by exact measurement. The basal cisterns normally vary in shape and size. The subarachnoidal air over the cerebral hemispheres gives anatomical informations of the sulci. Neither here can the exact metric dimensions be given. However, the sulci

should be quite narrow, and when air-filled they should appear in the roentgenogram as fine linear clearings."

(c): The possibility of performing direct measurements of the ventricular system and comparing them with the P.E.G. findings is found in autopsy examinations of the brain especially if intracranial fixation is as good as possible. A number of such examinations have been performed. *Elsberg and Silbert* (1925) made exact models of the ventricular system in patients with brain tumours and found by direct comparison with the P.E.G. findings close agreement.

Last and Tompsett (1953) made some beautiful models of the ventricular system and calculated the different sizes. On 24 brains they calculated Evans' ratio and found the mean value 0.26 (maximum 0.33 and minimum 0.21) with a standard deviation of 0.0339. The ventricular volume as compared to the cranial volume was found to be 0.016 (0.040-0.006). Mean value of the width of the third ventricle in the AP projection was 5.5 mm.

Weintraub (1953) stated in his thesis that two of his patients had P.E.G.'s performed and he found a close correlation between the autopsy findings and Evans' ratio. The problem of the changing size of the ventricular system with age was examined by *Morel and Wildi* (1953, 1954) who studied patients in a higher age group and found that over the age of 55 the capacity of the ventricular system increased until 80 and thereafter began to decrease. They found no difference in size between males and females until after 80 years of age.

Löken (1959) measured Engeset's SC-distance in 100 autopsied cases and found that it increased from approximately 6 mm. at 6 months of age to 9-10 mm. at 80 years and that this measurement was rather variable. Nevertheless this variation is almost parallel to the increase in cranial width in the age group covered (*Meredith* 1953, among others).

Knudsen's (1958) careful work on measurements of the ventricular size in normal adults includes information of the use of X-ray measuring methods. He showed that not all ventricular systems increase with age. In 48% of the examined brains the left lateral ventricle was larger than the right, and in 37% there was no side difference. (He calculated that anterior horns made up 35% of the total volume, that the central and temporal areas made up 48% and the posterior horn approximately 17%). The mean volume was only slightly greater in males than in females. As a result of statistical evaluation of the measurements he stated that one could hardly expect any greater correlation between linear or planimetric measurements and the ventricular volume.

Conclusion of survey of the literature with special reference to author's examinations.

The extensive literature on P.E.G. has shown a variable attitude to the examination. From the initial enthusiastic reports and general agreement on the value of the examination, especially with regard to brain tumours, this was followed in the thirties by a period when numerous attempts were made to use it in different fields and the conclusions were frequently exaggerated. In the forties reports were mainly of physiological reactions associated with insufflation. In the fifties a great number of P.E.G.'s were used for many different investigations and in making use of previous experience with regard to indications and contra-indications one continued to aim at reducing the risks as much as possible.

A similar tendency was present in the papers on P.E.G. in children. The number of reports was extensive, and was mainly concerned with disorders such as epilepsy, cerebral palsy and mental retardation. There have been very few studies on the prognostic value and in only a few cases has P.E.G. been related to follow-up examination.

The measuring methods applied can be divided into two major groups, planimetric measurements which are almost without practical use in clinical work and linear measurements. Linear measurements give exact figures which are only suited to adults whereas the use of a ratio or index is presumably the most useful in childhood. In the latter it is mainly based on measurement of the greatest width of the anterior horns or the cella media as compared with the external or internal cranial diameter.

The reliability and efficiency of such methods has often been discussed and except for a few isolated case reports one finds that the examination has not been reassessed by follow-up examination.

In a few cases attempts have been made to compare P.E.G.'s which have been repeated in order to obtain some idea of the reliability of the major methods.

CHAPTER III

Author's investigations

A: TERMINOLOGY

The term pneumoencephalography (P.E.G.) will be used for all forms of intracranial air insufflation regardless of method used. Ventriculography (V.E.G.), sub-occipital encephalography (S.E.G.) and lumbar encephalography (L.E.G.) are the three methods most commonly employed, but there are in addition other special types of P.E.G. where sub-dural spaces or cysts etc. are filled. These are rare however and have not been used in the present study.

The use of definitions has the advantage that it avoids misunderstanding. There is confusion in the literature as some authors use the term ventriculography as opposed to encephalography, and make no attempt to distinguish between S.E.G. and L.E.G. Other authors use the term encephalography or pneumoencephalography for all types of air insufflation and a few use aerography as a general classification. In several instances it is impossible to tell which method of insufflation has been used and it would therefore be advantageous to have a nomenclature which could be understood by all.

The term cerebral atrophy is not used unless it has been confirmed at operation or by histological examination. The use of the terms ventricular dilatation, dilatation of the sub-arachnoid space etc. is confined to the X-ray appearance and has nothing to do with the aetiology.

For similar reasons the use of the term internal hydrocephalus is avoided and ventricular dilatation used instead. Macrocephaly indicates a large head circumference, an analogue to the established terminology, microcephaly, and an abnormally large amount of fluid on the surface of the brain is described as dilated sub-arachnoid or sub-dural space.

In the present study, the ratio used for ventricular dilatation is that described by Evans: the greatest width of the anterior horns divided by the greatest internal cranial diameter on the anterior-posterior projection. The measurement is carried out for the whole system and everywhere this is the first figure mentioned. In addition a ratio has been obtained for each lateral ventricle by measuring these distances from the midline of the ventricular system and dividing the greatest width of each anterior horn by the corresponding distance from the midline to the internal cranial wall, thus obtaining the next two values (right side/left side). From the same measurements we obtain information as to whether the ventricular system is in the midline of the cranium or displaced to one side. If the difference in the distances between

the ventricular midline and the lateral walls of the cranium is greater than 4 mm. it is recorded. The side mentioned in connection with this difference indicates to which side the ventricular system is displaced.

In calculating the two ratios for the lateral ventricles only differences greater than 0.05 are recorded and this implies unequal lateral ventricles.

B: CRITERIA FOR THE PRESENT STUDY

Between 1934 when the Neurosurgical Department at the Rigshospital was established and July 1955 some 2,450 children were admitted. They fell into three main groups, viz. (1) 730 children with traumatic lesions, (2) 550 children with tumours or suspected tumours and (3) a large miscellaneous group consisting of 60 children with spinal disorders, 170 with infectious disorders, 460 with malformations, vascular disorders etc. and 260 with atrophic lesions.

The number of children admitted has increased steadily over the years from 63 in 1940 to 234 in 1948. Since 1948 the number of children admitted yearly has remained approximately the same. As will be seen from this study, the number of atrophic lesions has increased considerably in recent years and this can be related, among other things, to the fact that many patients who would have been admitted here in the past are now being treated at the more recently established neurosurgical departments in the country (*Busch* 1959).

The present material is composed of children admitted since the department's establishment in 1934 until July 1955, and consists partly of children with atrophic lesions, and partly of children with traumatic lesions where there is evidence of atrophy. In all 356 patients were studied but 48 were excluded because the diagnosis was not made on pneumoencephalography but on operative findings, arteriography or autopsy. In 21 patients it was impossible to measure the X-rays and a further 13 examinations were excluded because of technical difficulties. Of the remaining 274 children, 3 were excluded because they did not fulfil the criteria for a measurable ventricular dilatation. The final material consists of 271 children who fulfil the following criteria:

1. Under 15 years at the time of admission.
2. The disease was not diagnosed as brain tumour or acute infection.
3. All pneumoencephalograms were carried out in the Neurosurgical Department except for 13 patients where this study was undertaken in another department immediately before admission. All X-ray films were examined by neurosurgeons and were followed by further examinations, viz. operation, biopsy, arteriography etc.
4. At least one lateral ventricle on AP view was greater in width than one quarter of the distance from the midline to the internal cranial wall.

5. All patients were admitted before July 1955 so that there was at least one year's follow-up before the study began in the autumn of 1956.

C: AGE AND SEX DISTRIBUTION AMONG THE 271 PATIENTS

The age and sex distribution at the time of admission to the Neurosurgical Department is shown in Table 2 and Figure 3. It will be seen that there are more boys than girls and this has been observed by several others in reports concerning C.N.S. diseases in childhood, (*Stutte 1941, Andersen 1954, Vigouroux et al. 1954, Dyggve 1957, Skatvedt 1958, Bertelsen 1958, Thieffry et al. 1958*), and in older age-groups (*Bohn 1937, Magnussen 1950, Schwidde 1952, Lennartz 1954 and Decker and Nagel 1957*).

There is a preponderance of younger patients and this can be explained by the fact that in more recent years an increasing number of children were admitted to the Neurosurgical Department because P.E.G. in the paediatric service is not carried out in the form of ventriculography or S.E.G. and that the examination before one year of age is not performed as L.E.G. The increasing number can also be related to the changing character of admissions following the establishment of neurosurgical departments elsewhere.

The sex distribution in all age-groups shows a preponderance of boys.

D: SYMPTOMS ON ADMISSION TO THE NEUROSURGICAL DEPARTMENT

In collecting material based on pneumoencephalographic changes, one cannot expect it to represent a particular clinical picture because all patients who were not studied by P.E.G. or who had a normal or too small a ventricular system were excluded. This means that the only thing one can say is that among the 271 children with a ventricular system in which at least one lateral ventricle had a ratio of 0.25 or more, certain groups of symptoms were found and these symptoms frequently corresponded with the indications for the study being performed.

The signs and symptoms fall into four groups: (1) motor handicap, (2) epilepsy and (3) mental retardation which corresponds with what one would expect to find in children with presumed organic brain lesions and (4) a small group with other symptoms, e.g. headache, behaviour disorders, sight and speech disturbances. The various symptoms often occur in combination with one another.

Motor handicap alone was found in 17 children and with other signs and symptoms in 150 children. Epilepsy alone was found in 46 children and with other signs and symptoms in 134. In no case was mental retardation the only symptom but was always present with others, most frequently cerebral palsy and/or epilepsy. The last group consists of all other symptoms and they were the only disorders in 28 children.

Table 2

Age and sex distribution at time of admission to Neurosurgical Department

Age	Boys	Girls	Total
0- 1 month.....	2	0	2
1- 2 months.....	2	2	4
2- 3 -	3	1	4
3- 6 -	13	5	18
6- 9 -	16	6	22
9-12 -	15	9	24
1- 1 yr. 11 mths.....	22	20	42
2- 2 yrs. 11 mths.....	13	8	21
3- 3 -	10	7	17
4- 4 -	9	6	15
5- 5 -	4	3	7
6- 6 -	11	7	18
7- 7 -	4	4	8
8- 8 -	9	6	15
9- 9 -	4	4	8
10-10 -	11	3	14
11-11 -	6	2	8
12-12 -	4	1	5
13-13 -	7	5	12
14-14 -	6	1	7
Total..	171	100	271

Fig. 3.

SEX DISTRIBUTION AND AGE ON ADMISSION

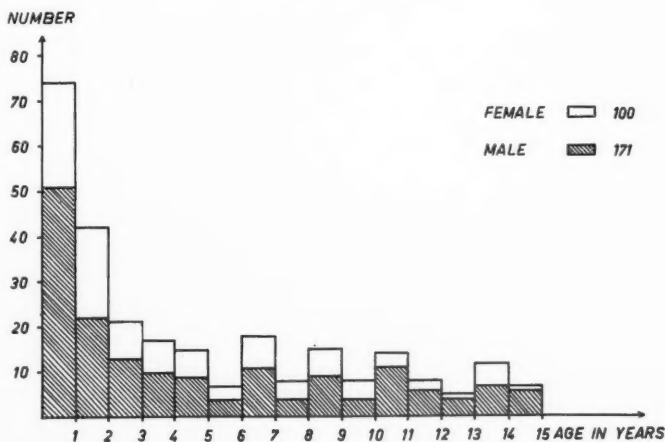


Table 3

Symptoms on admission to Neurosurgical Department

Three main groups of symptoms:

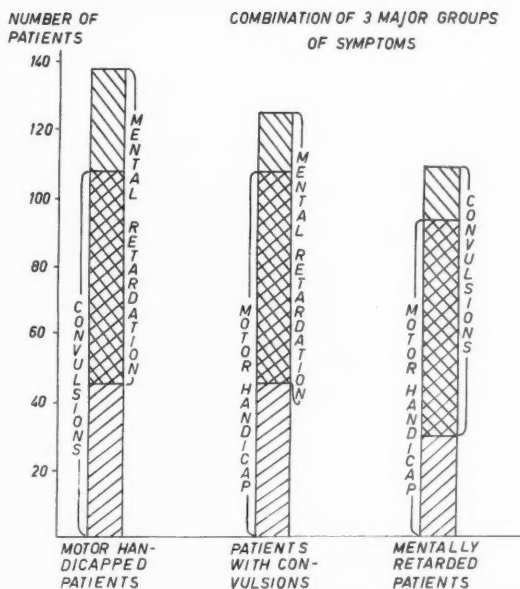
1. Motor retardation:	17 without other symptoms.	150 with other symptoms.
2. Convulsions:	46 — — —	134 — — —
3. Mental retardation:	0 — — —	113 — — —

In addition there were 28 patients with symptoms which fell outside the three main groups.

1. Motor retardation:	alone.	combined with other symptoms.
hemiplegia	5	52 (45 epileptic, 20 mentally retarded)
tetraplegia	1	26 (19 epileptic, 24 mentally retarded)
paraplegia	1	4 (1 epileptic, 3 mentally retarded)
rigidity	5	15 (10 epileptic, 7 mentally retarded)
motor retardation	1	37 (23 epileptic, 30 mentally retarded)
flaccidity	2	7 (4 epileptic, 5 mentally retarded)
other types	2	9 (6 epileptic, 4 mentally retarded)
2. Convulsions:	alone.	combined with other symptoms.
grand mal	19	61 (56 motor handicap, 36 mentally retarded)
petit mal	3	6 (5 motor handicap, 5 mentally retarded)
grand and petit mal	4	17 (9 motor handicap, 9 mentally retarded)
unilateral seizures	9	17 (14 motor handicap, 9 mentally retarded)
focal seizures	2	1 (1 motor handicap, 1 mentally retarded)
comb. other types	7	21 (14 motor handicap, 11 mentally retarded)
atypical (unknown?)	2	11 (9 motor handicap, 5 mentally retarded)
3. Mental retardation:	alone.	combined with other symptoms.
undefined retardation		54 (46 motor symptoms, 35 epileptic)
slight defect		13 (10 motor symptoms, 9 epileptic)
severe retardation		13 (12 motor symptoms, 11 epileptic)
I.Q. 76-90		3 (1 motor symptoms, 2 epileptic)
I.Q. 56-75		11 (7 motor symptoms, 8 epileptic)
I.Q. 36-55		14 (12 motor symptoms, 11 epileptic)
I.Q. 0-35		5 (5 motor symptoms, 2 epileptic)
The symptoms in the 28 patients not included in the three main groups were as follows:		
headache	12	
behaviour problems, irritability	4	
increased cranial circumference	3	
eye symptoms	4	
miscellaneous (e.g. pubertas præcox, obesity, fractured skull, dizziness etc.)	5	

Table 3 shows the various symptoms and sub-groups and the different combinations. Fig. 4 shows how frequently the three main groups are combined with one another. It will be observed that cerebral palsy, epilepsy and mental retardation were found in 63 children and cerebral palsy combined with either convulsions or mental retardation in 136 children. Epilepsy combined with cerebral palsy and mental retardation was found in 124 children and, finally, mental retardation combined with cerebral palsy or convulsions in 109.

Fig. 4.



No attempt has been made to decide which symptom was the most important. It would be difficult to say if slight mental retardation or convulsions is the more important indication for P.E.G. Nevertheless, there are certain observations which give some idea of the above-mentioned problem, for instance the fact that mental retardation is never the only symptom. This could be interpreted as meaning that this condition has to be combined with some other condition before P.E.G. is considered justifiable. Another finding is that a large number of children had some form of convulsion, viz. 180 (66%). This could be interpreted that this symptom was a major indication for P.E.G. Similarly the relatively high number of patients with hemiplegia, either alone or combined with other symptoms, suggests that this condition was another major indication for P.E.G.

Among the many different combinations of symptoms and signs one sees in motor handicapped patients for instance, there appears to be a close correlation between hemiplegia and epilepsy, and between tetraplegia and mental retardation, though convulsions are also found combined with the last two conditions. Of the different types of convulsions grand mal is as usual the most frequent.

Those patients with the most severe retardation often have multiple symptoms with motor handicaps as well as convulsions. Whether one should consider the retarded motor development which is often associated with the mental retardation as a sub-group of cerebral palsy is a question of definition.

Cerebral palsy, epilepsy and mental retardation were the predominant conditions in this material (only 28 children have not had one or more of these conditions). This was to be expected from the selection of the material on the pneumoencephalographic findings as it has been shown by *Salomonsen, Eek and Skatvedt* 1957, among others, that the pneumoencephalographic appearance in these disorders is almost the same.

E: THE TIME OF RECOGNITION OF THE DISEASE

From the symptoms it will be seen that we are frequently dealing with very serious conditions. This is further supported by the fact that many of the disorders are recognised at birth or soon afterwards.

In only 9 children it was impossible to determine the time of recognition of the disease, and in a further 3 children it could only be placed as being prior to the age of 3 months. In the remainder of the material it was possible to determine the time of the disease's onset. In some children it was when the parents first noticed that something was wrong and this could have been rather late in the disease.

Table 4
Time of recognition of disease

Age	Total
<24 hrs.....	66
24 hrs.-2 mths.....	43
3 mths.-5 mths.....	16
6 mths.-11 mths.....	33
1 yr.-2 yrs. 11 mths.	35
3 yrs.- 5 yrs. 11 mths.....	29
6 yrs.- 8 yrs. 11 mths.....	20
9 yrs.-13 yrs. 11 mths.....	20
	262
No information.....	9
Total..	271

From Table 4 it will be seen that 66 children had symptoms which were evident within the first twenty-four hours of life, 59 had symptoms which were noticeable during the first six months of life and 158 were recognised before one year of age. In 20 children the condition was recognised after nine years of age.

F: AETIOLOGY

Information regarding aetiology in the 271 cases is based on the records from the Neurosurgical Department as well as other departments, and is

supplemented as much as possible by the information collected at follow-up. The results of a retrospective enquiry should always be carefully evaluated because some of the information obtained several years after admission could be influenced by the fact that the same questions have been asked so often that it has affected the answers. Furthermore, many parents may possibly have read the popular press to further their knowledge of their children's condition (*Fuglsang-Frederiksen* 1958). Keeping this point in mind the following has to be considered:

Information regarding aetiology was obtained in 247 cases and distribution is as follows:

Familial history of disease:	52 patients
Prenatal factors:	50 patients
Perinatal factors:	153 patients
Postnatal factors:	112 patients

Of the 247 patients studied a single aetiological factor was present in 145 cases (59%), two factors in 84 patients and three factors in 8 patients. A combination of the different aetiological factors can be seen in Table 5.

Table 5
Possible aetiological factors

	Familial predisposition	Prenatal	Perinatal	Postnatal	Familial predisposition and prenatal	Perinatal and postnatal
Familial predisposition....	6	6	18	11		7
Prenatal factors	6	6	21	6		7
Perinatal factors.....	18	21	75	22	3	
Postnatal factors	11	6	22	58	1	

The possibility of a multiple aetiology is found in 41% of the cases. The same criteria has been applied to brain-damaged patients in ten years' autopsy material from an American institution for mentally retarded (Walter E. Fernald State School) made up of all age-groups and based solely on information from the records. The material consisted of 174 patients, 36 of which were excluded because of insufficient information regarding aetiology, and of the remaining 138, 49 (36%) had more than one aetiological factor.

When only one aetiological factor is present this is specified and when more than one factor is present the author has tried, wherever possible, from information contained in the records as well as that obtained at follow-up examination, to evaluate the importance of the individual factors. In a large number of cases this was impossible to determine.

Table 6

Familial predisposition to neuro-psychiatric factors

	Familial predisposition			
	Only information	Of major or equal importance	Of minor importance	Total information
Mother and/or father mentally retarded	2	2	0	4
Mother and/or father with convulsions..	0	6	4	10
Mother and/or father and possibly other close relations with mental disorders...	0	2	3	5
Siblings:				
oligophrenia.....	1	1	2	4
convulsions.....	0	3	0	3
paraplegia.....	0	1	0	1
cranial malformations.....	0	1	0	1
deafness.....	0	2	0	2
congenital cataract.....	1	0	0	1
First cousins:				
oligophrenia.....	1	1	6	8
Grandparents, parents' siblings:				
convulsions.....	0	3	9	12
Parents' siblings:				
dementia praecox.....	1	0	0	1

Hereditary and familial factors (Table 6): hereditary and familial factors are restricted to central nervous system disorders in parents, grandparents, siblings, first cousins and parents' siblings. Headache, slight nervousness or similar common and ill-defined symptoms have been excluded. The central nervous system disorders considered were convulsions, intellectual inferiority, oligophrenia, schizophrenia and dementia praecox. In a few cases information regarding special disorders among siblings is available, viz. defects of vision, deafness etc., and this can provide an explanation where otherwise none would be forthcoming.

In 6 patients the only aetiological information was on familial predisposition and in 46 patients other aetiological factors were also present. A family history of convulsions was found in 25 patients, occurring in siblings and parents in 13 cases and in more distant relatives in 12. This means that in this material approximately 10% had a family history of convulsions which is considerably higher than that found by E.E.G. examination concerning the inheritance of epilepsy (5.1%), (Harvald 1954). The figure is more in agreement with the 9.4% reported by Eisner *et al.* in 1960.

Oligophrenia and intellectual inferiority was also present in siblings and parents in 8 cases and in more distant relatives in 8 cases, i.e. 7%.

Prenatal factors: it is not the intention of this study to mention all aetiological factors within the different clinical syndromes, such as the influence of pre- and perinatal factors as a great number of reports, including Danish

material, deal with these problems, e.g. *Wildenskov* (1934), *Faber* (1947), *Anderson* (1952), *Olsen* (1955), *Kærn* (1955), *Plum* (1956, 1957, 1958), *Masland et al.* (1958), *Hansen* (1960). The patients in this material have been selected according to P.E.G. findings so that no connection can be established between any one aetiological factor and a clinical entity. Only information concerning aetiology in groups of patients with the same P.E.G. findings and similar clinical pictures can be obtained. With regard to information concerning prenatal damage, the same uncertainty arises as with all retrospective information, and we hope to obtain more valid information from the prospective study which is now taking place.

The information regarding diseases of pregnancy shows that hypertension, oedema and nausea are predominant, and to this group must be added three mothers with an ill-defined history of "pregnancy intoxication." Information regarding infections is just as uncertain, e.g. in the case of influenza it will presumably always be possible in material covering any number of patients to find mothers who had influenza outside the true epidemic periods. On the other hand, one cannot reject the possibility that such information is of equal importance as that on German measles.

Table 7 shows the information obtained, and it can be seen that in only 6 cases was the prenatal factor the only factor but in combination with other factors it occurred in 44 cases. Of this number the prenatal factor was judged to be of major importance in 37 cases, so that the prenatal influence was of definite or possible importance in 15% of the 247 reported cases.

Table 7
Possible prenatal factors

	Prenatal factors alone	Prenatal factors of major or equal importance	Prenatal factors of minor importance	Total
Hypertension with albuminuria, oedema, severe vomiting, "toxaemia of pregnancy"	2	20	4	26
Pyuria/pyelitis	2	2	0	4
Twin death in utero	1	0	0	1
Shock	1	0	0	1
Pain	0	3	0	3
Haemorrhage	0	4	1	5
Vaginal discharge	0	2	0	2
Injury	0	1	0	1
Descended uterus	0	0	1	1
Hormone injection	0	1	0	1
Infection	0	4	1	5
		(1 syphilis) (1 toxoplasmosis) (2 influenza)	(German measles?)	

Perinatal factors: prematurity can be considered a transitional aetiological factor between prenatal and perinatal sequelae because it frequently results from an unstable or complicated pregnancy, and because it often leads to asphyxia, jaundice etc. Information on birth weight was obtained in 255 children of whom 32 weighed $\leq 2,500$ g. Low birth weight was the sole aetiological factor in 11 cases and combined with other factors in 21 cases. Severe asphyxia was found in 6 cases. It is to be noted that the number of children with low birth weight is approximately twice as great as would be expected from *Nørregaard's* report on prematurity frequency i.e. 6.5%, but is considerably smaller than the figures obtained for cerebral palsy by *Plum* (1956) and *Brandt and Westergaard-Nielsen* (1956).

The distribution of birth weight can be seen from the following figures:—

Birth weight	Prematurity	
	Alone	Combined with other factors
2,500 g.	2	2
2,000–2,499 g.	5	10
1,500–1,999 g.	4	6
< 1,500 g.	0	1
No information	0	2
Total	11	21

Before considering true perinatal factors there were 3 patients on whom the only information obtained was that the birth was too early but where the birth weight was above 2,500 g. These patients have been included in the perinatal group but could possibly equally well have been placed in the group on which we had no information.

Birth injuries: asphyxia is the most frequent factor and was seen in 40 patients 6 in 19 of whom it was prolonged (> 15 minutes), 6 of short duration, and in 15 there was no information on the time involved. In 30 patients there was a history of prolonged labour and delivery; difficult birth was found in 13. Furthermore, we have information on forceps delivery in 2, breech presentation and other pathological presentations in 3, Caesarian section in one, and in none of these were there perinatal complications of the types already discussed. Ten of the births were induced medically and in another 10 delivery was precipitate. In addition, information on less common factors is available in Table 8. Perinatal factors alone were found in 60 patients. In 4 patients there was a history of prematurity and delivery complications, and combinations of other factors were found in 63 patients. The assessment of the significance of perinatal factors in combination with other factors was very difficult, especially with regard to postnatal diseases. However, the number of patients in whom perinatal factors are of prime importance was approximately 100 (40%).

Table 8
Possible perinatal factors

	Alone	Combined with		Total
		Familial predisposition and/or prenatal factors	Postnatal factors, and possibly familial predisposition and prenatal factors	
Asphyxiation of more than 15 minutes..	12	7	0	19
Asphyxiation, brief.....	3	1	2	6
Asphyxiation, duration unknown.....	7	5	3	15
Protracted birth.....	17	13	0	30
Difficult birth.....	0	0	13	13
Forceps delivery.....	0	0	2	2
Breech presentation and other pathological positions.....	0	3	0	3
Caesarean section.....	1	0	0	1
Medically induced labour.....	5	3	2	10
Precipitate delivery.....	5	4	1	10
High birth weight, ≥ 4500 g.....	1	0	2	3
Prolonged icterus.....	3	1	0	4
Ingestion of amniotic fluid.....	1	0	0	1
Obvious pressure marks.....	2	0	0	2
Said to be premature but birth weight above 2500 g.....	3	0	1	4

Postnatal factors: these fall into two main groups, post-traumatic and post-infectious. Head injury was the only aetiological factor in 36 cases, and combined with other possibilities was present in 24. The frequency of head injury in this material was 24% which compares with the findings in similar groups of patients with disorders of the central nervous system (*Otto 1960, Melchior 1961*).

Sequelae following infectious diseases was the sole aetiological factor in 17 cases and two more patients with ear disease might be added. Infection was present in combination with other factors in 18 cases bringing the total to 37. Of the 17 patients with post-infectious sequelae, the infectious disease in 5 was due to meningitis (pneumococcal, tuberculous etc.), and in two was due to severe lung infection with meningeal symptoms. Of the remainder an unexplained high fever was present in 10 patients and gastroenteritis was the cause of the fever in two. An upper respiratory tract infection accompanied by febrile convulsions was the cause in 3 patients and in 3 patients the disease began after whooping-cough.

No information on possible aetiology: this covers 24 cases. In 6 of the case records there was a family history available but the information was so uncertain that it was not considered relevant. In this group of patients the best guide to a possible aetiology was the time at which the disease occurred. Ten patients developed symptoms before one year of age and in only 6 cases the symptoms appeared after 2-3 years of age.

Summary of symptoms, time of recognition and aetiology of disease: The symptoms fall mainly into 3 groups: motor handicap consisting of cerebral palsy and retarded motor development, epilepsy and mental retardation which covers both intellectual inferiority and oligophrenia.

A great number of children in the present material had symptoms early, i.e. within the first twenty-four hours, and 58% of the patients had symptoms before one year of age.

The aetiological factors may be subdivided into four major groups: (1) approximately 10% with a family history of disease, (2) 15% with possible prenatal damage, (3) 40% with perinatal and (4) 40% with postnatal damage. More than one factor was present in 41%.

G: METHOD OF EVALUATING PNEUMOENCEPHALOGRAPHIC CHANGES

In all the 271 cases P.E.G. showed a well-filled ventricular system. This was a criteria for inclusion in this study. The author was anxious to determine if the degree of dilatation was of prognostic significance. For this purpose Evans' ratio, with some modifications, was used to assess the dilatation of the ventricle. This ratio was preferred because Evans' original work was based on paediatric material, and because it was justified to consider it independent of age. As mentioned in the section on measuring methods (p. 48) it was a requirement for using figures that these should be relative and not exact, one of the reasons for this being the marked increase in head circumference which takes place in the first year of life (from 35-46 cm.) and which is followed by a constant but smaller increase year by year.

Evans' ratio is the greatest width of the anterior horns divided by the greatest internal cranial diameter on the AP projection. The normal value is 0.25, possible dilatation between 0.25 and 0.29 and a value of 0.30 indicates definite dilatation. The ratio does not show whether there is asymmetrical dilatation or displacement of the ventricular system, and for this reason the author chose to measure the ratio for each side as well as the ratio for the whole system. This measurement is calculated from the midline of the ventricular system. All X-ray films have been seen several times by the examiner, and measurement carried out with millimetre rulers. In this way the margin of error is less than 1 mm. A 1 mm. difference in breadth will alter the ratio approximately 0.01 if it is the anterior horn measurement which is changed, whereas a difference of 1 mm. in the cranial diameter will have less influence on the ratio. The internal cranial diameter is easily determined. Nevertheless, doubt will occasionally arise but when one is considering the slight influence a change of approximately 1 mm. will produce even a small error will not change the values to any great extent.

By measuring each half of the ventricular system it is possible to indicate the difference in ratio of the two sides as well as the displacement of the ventricular system to one side. A difference of 1 mm. in the anterior horn width will alter the ratio 0.01 on each side and a difference greater than

0.05 is considered necessary before attaching any importance to it. The exact midline of the ventricular system was not always easy to determine and therefore the difference in distance between the midline and the internal cranial wall on the two sides was 5 mm. before the ventricular system was considered to be displaced. These calculations have the advantage that they can be made during the daily clinical work by means of simple rulers.

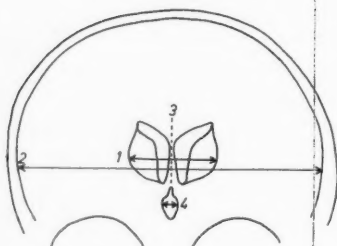
In addition to the above ratio, the width of the third ventricle was measured in the AP projection, and the amount of cortical air was assessed. As may be seen from the literature, this is a difficult procedure in children. It has been necessary, therefore, to employ definite criteria for describing cortical air as exact measurements cannot be used in childhood. For instance, if we talk about broad sulci it is necessary for these changes to be found in more than one picture and for them to be in the same position on repeated examinations. It is possible to divide the findings into three groups: (1) diffuse air collection over both hemispheres, (2) air over one hemisphere alone and (3) localised collection of air. This last finding was seen frequently with the aforementioned two. Cortical air on one or both sides, showing well-defined, thin sulci was not considered abnormal. On the contrary, this indicates a normal cortical surface. In the present material, where one of the criteria has been a well-filled ventricular system, there has been no doubt as regards the cortical air findings.

The presence of cysts, porencephaly, agenesis of the corpus callosum, cysts in the septum pellucidum, or similar findings, have been described individually.

The evaluation of the films corresponding to the above-mentioned criteria was based on the following: (Fig. 5).

1. Filling of the ventricular system on AP projection:
 - (a) Measurement of the internal cranial diameter.
 - (b) Measurement of the greatest width of the anterior horns.
 From this is calculated Evans' ratio for the whole system.
2. By measuring the distance from the ventricular system's midline to the internal cranial wall, and the greatest width of the anterior horns, the following can be calculated:
 - (a) The ratio for each lateral ventricle.
 - (b) The possible displacement of the ventricular system.
3. Measurement of the width of the third ventricle on AP projection.
4. Evaluation of the air on the surface of the hemisphere with reference to:
 - (a) Normal distribution.
 - (b) Abnormal distribution which could be seen as
 - (i) Sub-arachnoid:
localised, unilateral or generalised.
 - (ii) Sub-dural air.
5. Special findings.

Fig. 5.
Case No. 40.



OWN MEASUREMENTS.

- 1: TRANSVERSE DIAMETER OF THE ANTERIOR HORNS.
- 2: INTERNAL TRANSVERSE DIAMETER OF THE SKULL.
- 3: MIDLINE OF THE VENTRICULAR SYSTEM.
- 4: TRANSVERSE DIAMETER OF THE 3. VENTRICLE.

By using these measurements it was possible to divide the material into bilateral and unilateral ventricular dilatations. Bilateral dilatation was subdivided as follows:

Bilateral dilatation with the same ratio on each side and no displacement of the ventricular system.

Bilateral dilatation with the same ratio on each side with displacement of the ventricular system.

Bilateral dilatation with different ratios on each side and no displacement of the ventricular system.

Bilateral dilatation with different ratios on each side with displacement of the ventricular system.

The reason for choosing these definitions for the different types of changes which can be seen in bilateral ventricular dilatation was that more precise information could be obtained than when the terms symmetrical or asymmetrical systems were used. In this material bilateral dilatation with no displacement of the ventricular system, and with the same ratio on each side, means that there was almost symmetrical dilatation because, as defined above, the difference in the ratios on the two sides must not be > 0.05 , and the system's midline should not be displaced > 4 mm. This means that all other types of bilateral dilatation were asymmetrical and this seems to be too much of a generalisation as will be shown below. Dilatation with displacement of

the ventricular system and unequal ratios is composed of two conditions: (1) The displacement of the ventricular system may be to the same side as the smallest ventricle. In this case the ratio will often be almost the same on the two sides. (2) The smallest distance from the ventricular system midline to the cranial wall will be on the same side as the largest lateral ventricle, in which case the difference in ratio will be marked. By indicating the displacement of the system by number and side it is possible from the figures to make a drawing of the ventricular system in each case. Unilateral ventricular dilatation means that only one lateral ventricle measures > 0.25 . In the present material unilateral ventricular dilatations formed a small group, some with no displacement and some with displacement of more than 5 mm. Displacement of the ventricular system is again indicated by side. A minus figure means that on a given side the distance to the cranial wall is that much less than the other side. The figure thus obtained is the difference between the two sides.

The 271 patients are distributed in the above-mentioned groups as follows:

Equal dilatation of the ventricular system without displacement was found in 152 patients (cases no. 1-152), and the ratios were measured to:

0.25-0.29	21 patients	Fig. 6
0.30-0.34	63 patients	Figs. 7, 18, 21, 23, 25, 26
0.35-0.39	41 patients	Figs. 8, 19, 20, 22
0.40-0.49	17 patients	
0.50 and above	10 patients	Fig. 9

Bilateral dilatation with the same ratio on both sides and displacement of the ventricular system was found in 31 patients (cases no. 153-183). The ratios were:

0.30-0.34	17 patients	Fig. 10
0.35-0.39	8 patients	Fig. 11
0.40-0.49	3 patients	
0.50 and above	3 patients	

Unilateral dilatations were found in 6 patients with no displacement of the ventricular system and 8 with displacement (cases no. 184-197). The ratios were:

≤ 0.29	12 patients	
0.30-0.34	1 patient	Fig. 12
0.35-0.39	1 patient	

Bilateral dilatation with a difference between the two sides of > 0.05 was found in 34 patients without displacement of the ventricular system (cases no. 198-231), and the ratios were:

0.25-0.29	3 patients	Fig. 13
0.30-0.34	10 patients	Figs. 37, 38, 39
0.35-0.39	8 patients	
0.40-0.49	10 patients	
0.50 and above	3 patients	

Finally, displacement of the ventricular system and a difference in ratio of > 0.05 was found in 40 children (cases no. 232-271). The ratios were:

0.25-0.29	1 patient	
0.30-0.34	14 patients	Fig. 14
0.35-0.39	6 patients	
0.40-0.49	9 patients	Fig. 15
0.50 and above	10 patients	Figs. 16, 17

It was possible to measure the diameter of the third ventricle in 235 of the examined cases, and it was found to vary between 2 and 26 mm. The figures are seen below:

Ventricular diameter	2 mm.	11 patients
	3 mm.	29 patients
	4 mm.	35 patients
	5 mm.	31 patients
	6 mm.	32 patients
	7 mm.	24 patients
	8 mm.	21 patients
	9 mm.	10 patients
	10 mm.	10 patients
	11 mm.	8 patients
	12 mm.	8 patients
	13 mm.	4 patients
	14 mm.	5 patients
	15 mm.	2 patients
	16 mm.	1 patient
	17 mm.	1 patient
	20 mm.	1 patient
	21 mm.	1 patient
	26 mm.	1 patient

Cortical air in abnormal amounts was found in 48 cases of which 23 showed diffuse cortical air (Figs. 8, 15), 7 showed unilateral cortical air and 18 localised collections (Figs. 10, 13, 18).

Table 9

Distribution of the 271 patients according to their P.E.G. findings, type, size of ratio and presence of cortical changes

Type of ventricular dilatation	Ratio	No.	Cortical changes			
			gen.	unilateral	localised	total
Bilateral	0.25-0.29	21	0	1	1	2
no ratio diff.	0.30-0.34	63	2	2	6	10
> 0.05	0.35-0.39	41	8	0	4	12
no displacement	0.40-0.49	17	3	0	1	4
≥ 5 mm.	≥0.50	10	0	0	0	0
		152	28			
Bilateral	0.25-0.29	0	0	0	0	0
no ratio diff.	0.30-0.34	17	2	0	0	2
> 0.05	0.35-0.39	8	1	0	0	1
with displacement	0.40-0.49	3	0	0	1	1
≥ 5 mm.	≥0.50	3	1	0	0	1
		31	5			
Unilateral	only one ratio					
no displ. ≥5mm.	≥0.25	6	0	1	0	1
with displ. ≥5 mm.		8	0	0	0	0
		14	1			
Bilateral	0.25-0.29	3	0	1	0	1
with ratio diff.	0.30-0.34	10	0	1	0	1
> 0.05	0.35-0.39	8	1	0	1	2
no displacement	0.40-0.49	10	0	0	3	3
≥ 5 mm.	≥0.50	3	1	0	0	1
		34	8			
Bilateral	0.25-0.29	1	0	0	0	0
with ratio diff.	0.30-0.34	14	0	0	0	0
> 0.05	0.35-0.39	6	0	0	1	1
with displacement	0.40-0.49	9	2	1	0	3
≥ 5 mm.	≥0.50	10	2	0	0	2
		40	6			
		271	48			

Special findings consist of porencephaly (Figs. 18, 19) in 4 patients and agenesis of the corpus callosum in one patient.

Cysts of the septum pellucidum were actually seen in 2 cases (Fig. 20), and non-communicating cysts (Fig. 21) were presumed to be present in 5

patients. One patient was suspected of having a Verga cyst. Sub-dural air collections were found in 9 patients. Table 9 shows the distribution of ratios among the five main groups, and the presence of cortical changes.

In cases where the lateral ventricles showed different ratios it was found that the left ventricle was larger than the right in 67 cases and the reverse was found in 16 patients. This gives a ratio of 4:1. The difference in distance is seen from the following:

	0.06-0.09	0.10-0.14	0.15-0.19	≥ 0.20
Left:	43	12	6	6
Right:	6	5	2	3

The finding that the left side was larger than the right has been mentioned in a number of reports, *Abramowitsch and Winkler* (1930), *Simonsen* (1951), *Heidrich* (1955), *Kohler* (1957), *Knudsen* (1958), *Bruijn* (1959), among others.

Simonsen emphasised that one must take into consideration the position of the head during birth as it is usually in what is called the first head position that the left hemisphere is more exposed to trauma than the right. The problem of dominant hemisphere versus non-dominant hemisphere has also been mentioned in this connection.

H: REACTIONS TO PNEUMOENCEPHALOGRAPHY

One of the problems which was investigated was the question of whether children, especially those with presumed severe brain damage, could withstand P.E.G. as well as adults, and to what extent complications were found. As seen from the literature, a rise in temperature is an almost constant finding in P.E.G. of any kind, successful or unsuccessful. This rise, together with a number of other symptoms, is thought to be due to a neurovegetative reaction of the C.N.S. to the procedure, (*Bohn* 1937, *Delay et al.* 1944, 1945c, *Kautzky* and *Burchard* 1950, *Kuhlendahl* 1950, *Frowein and Harrer* 1950, *Hockerts and Böcking* 1950, *Boudin, Barbizet and Leprat* 1954).

More serious complications with fatal results have been described in a number of cases (see survey p. 26). The patients in this material have almost invariably had V.E.G. or S.E.G. and only a few L.E.G. This is due to the fact that routine examination in the Neurosurgical Department was S.E.G. for many years, following *Busch's* method, if V.E.G. was not used. Another reason was the fact that a number of patients were examined before admission in other departments by L.E.G. which was frequently unsuccessful, and thus necessitating an alternative form of insufflation.

Altogether 159 ventriculographies had been performed of which 7 were unsuccessful, but of these 2 were repeated later with a good result. Of the 152 cases showing filling of the ventricular system the temperature was raised in 118, i.e. morning temperature above 37.5° C. and/or evening temperature above 37.8° C. Complications other than fever were seen in 20 cases, 5 had

headache, 2 were irritable, 7 showed signs of latent or manifest shock with a feeble pulse, rapid respiration, pallor etc., and 5 patients had neck stiffness. In one case there was leakage of C.S.F. following examination. There were no deaths among the 149 patients. Of the complications encountered 13 occurred among the 118 patients who had a fever and 7 among the 34 patients who were afebrile. S.E.G. was performed on 131 occasions, 13 of which were unsuccessful. In the 118 examinations febrile reactions were seen in 68 patients, other complications in 11 and there were 2 deaths which could be related to the examination. Complications occurring in 11 patients were made up of 5 with headache and vomiting, one with bleeding after examination, 2 with latent shock, 2 with neck stiffness and one with cessation of respiration for a short period. Nine of these complications were associated with a raised temperature.

Very few lumbar encephalograms were performed and, therefore, it is not possible to assess the reactions. Three patients were examined by this method and no complications occurred after the examination.

A febrile reaction, as can be seen from the above, is a frequent occurrence after P.E.G., and is seen in about 75% of the patients after V.E.G. and 60% after S.E.G.

Tables 10 and 11 show the degree and duration of temperature elevation, and the relationship of the fever to the size of the ratios. It is seen from the Tables that there is no particular difference between the reactions to V.E.G. or S.E.G. Very high temperatures are rare in both groups, and there is no difference in reaction between boys and girls. 74 of 118 febrile V.E.G.'s and 44 of 68 febrile S.E.G.'s were in boys which exactly corresponds with the number calculated for the sex distribution in the whole material. It is seen that the distribution of the febrile reaction does not alter with the altered ratios.

Table 10
Rise in temperature

Ratio	Total in whole material	V.E.G.					S.E.G.				
		Total with fever	Temp. < 38°c.	38°c.-38.9°c.	39°c.-39.9°c.	≥ 40°c.	Total with fever	Temp. < 38°c.	38°c.-38.9°c.	39°c.-39.9°c.	≥ 40°c.
0.25-0.29	37	10	1	9 (1)			15	1	13 (2)		1
0.30-0.34	105	41	1	33 (3)	7 (1)		27	3	18	6	
0.35-0.39	64	32	3	24 (1)	2	3 (1)	15	1	10	4 (2)	
0.40-0.49	39	21	4	9 (2)	6	2 (2)	9		9 (1)		
≥ 0.50	26	14	2	9 (2)	2	1	2		2		
Total..	271	118	11	84 (9)	17 (1)	6 (3)	68	5	52 (3)	10 (2)	1

(The figure in brackets indicates the number of patients included in the first figure who had other complications).

Table 11
Duration of fever

Ratio	V.E.G.					S.E.G.				
	Total with fever	<24 hrs.	24-48 hrs.	48-72 hrs.	>72 hrs.	Total with fever	<24 hrs.	24-48 hrs.	48-72 hrs.	>72 hrs.
0.25-0.29	10	7 (1)	2	1	1	15	13 (1)	1 (1)		1
0.30-0.34	41	26 (2)	8 (1)	4 (1)	3	27	17	4	5	1
0.35-0.39	32	12	11	3 (1)	6 (1)	15	11 (1)	2	1	1 (1)
0.40-0.49	21	12 (1)	5 (2)	1 (1)	3	9	7	2 (1)		
>0.50	14	6	2 (1)	1	5 (1)	2	2			
Total..	118	63 (4)	28 (4)	10 (3)	17 (2)	68	50 (2)	9 (2)	6	3 (1)

(The figure in brackets indicates the number of patients included in the first figure who had other complications).

I: DEATHS FOLLOWING S.E.G.

Among the 118 S.E.G.'s performed there were 2 deaths.

The first was a boy (case no. 121) aged one year and four months. During pregnancy the mother developed hypertension and eclampsia. Birth weight was 2,100 g. Gastroenteritis developed immediately after birth and the child was in hospital for 3½ months. He was seen to be physically handicapped when he was 10 months old, and the left side was particularly affected. At the age of 15 months he could not sit alone and was mentally retarded. A squint was present and there was a left Babinski. X-ray of the skull showed no abnormality. S.E.G. revealed a ratio of 0.39 (0.37/0.42). Third ventricle was 11 mm. (Fig. 22). Bilateral burr holes revealed clear fluid and thickened arachnoid. The patient did not awaken until the next morning, and then for only a short time. Death followed immediately after this.

Autopsy revealed hyperaemia and oedema. The brain was extensively damaged during removal. There was moderate ventricular dilatation corresponding to the S.E.G. findings. The pons and cerebellum were normal macroscopically. The only tissue which could be examined microscopically was the medulla which was found to be hyperaemic and without signs of infection.

The second patient (case no. 43) was a girl aged 2 years whose birth was difficult. Birth weight was 3,750 g. Shortly after birth it was noticed that she had hyperextended ankle joints. She walked alone at 18 months. Following a head injury at that time she suffered from headache and increasing gait difficulties. On physical examination she was found to have a spastic paraplegia. Examination of the eyes, E.E.G. and lumbar myelography were normal. S.E.G. ratio was 0.32 (0.32/0.33). Third ventricle was 10 mm. The films did not allow a definite evaluation of the condition of the posterior fossa (Fig. 23).

Following examination the patient developed hyperpyrexia and brain stem convulsions and died. Autopsy was not permitted.

Two deaths are not many if one considers how severely ill most of the children were at the time of admission. Furthermore, it is not always correct to blame the examination for the death as can be seen from the report on a case from Argentina (*Gherzi* 1946), in which a patient who was to have a P.E.G. died one hour before the examination from an intercerebral haemorrhage.

The same fact is illustrated by the following case reports of two children on whom it was intended to carry out P.E.G. but who died before examination. Such deaths could easily have happened a little later and influenced the mortality rates for the examination.

1. Case history: case record no. 06542/50. Male born 22.9.50. No known relevant family history. Only child. Pregnancy and birth normal. No asphyxia but patient did not cry until injections and other manipulations were tried. Birth weight was 3,550 g. The day after birth the child had clonic convulsions involving all extremities and was admitted to the paediatric ward where he was found to be in poor general condition and having almost continuous convulsions. Lumbar puncture revealed xanthochromic fluid containing erythrocytes. When six weeks old he had generalised convulsions, was stiff and had opisthotonus. Treatment with phenobarbitone was started. Subdural puncture showed 2-3 ml yellow, slightly bloodstained fluid. At the time of admission to the Neurosurgical Department in November 1950 his general condition was poor. He had a cold and diarrhoea and vomiting. This was not thought to be due to any acute cerebral disorder and the child was seen by a paediatrician who thought the condition was probably a paralytic ileus and transferred him to the Paediatric Department where he died the same day. Autopsy showed ileus and peritonitis. Brain autopsy showed polyporencephaly.

2. Case history: case record no. 08902a/52. Male born 9.7.51. No known relevant family history. Only child. Pregnancy normal. Birth medically induced but otherwise normal. The patient had no immediate symptoms and the birth weight was 3,250 g. Shortly after birth it was noticed that his extremities were stiff and there was a tendency to assume the opisthotonus position. From the age of one month he had convulsions, usually tonic and occurring in series several times a day. They commenced with a high-pitched cry, the patient stiffened and his eyes rolled up. He was admitted to the paediatric ward in November 1951. Eye examination showed no abnormality. E.E.G. was grossly abnormal with diffuse spikes and waves of the "hypsarrhythmia type". Bilateral subdural puncture revealed bloodstained fluid. He was admitted to the Neurosurgical Department 2.2.52. The skull was found to be egg-shaped with a circumference of 45.5 cm. He could not lift his head, sit or focus. He was pale and obese. He developed pneumonia and was transferred to the paediatric ward. He was readmitted to the Neurosurgical Department

in March 1952 after being at home for a short while. On physical examination the eye condition was still normal. P.E.G. was ordered but before this could be carried out the patient died.

Autopsy revealed congenital dysplasia of the brain, perivascular encephalomalacia and pulmonary atelectasis.

J: OTHER EXAMINATIONS

Other examinations including serological studies for syphilis and, in later years, examination for toxoplasmosis and blood incompatibilities have been negative except for one or two cases. These can be seen in the case reports and the aetiological tables.

Two examinations which have been carried out in a great number of cases may have possible prognostic value, viz. X-ray examination of the skull and electroencephalography. The latter examination was not performed in earlier years because the department lacked the facilities.

X-ray of the skull: this was performed on 186 children while in hospital and on 85 either during P.E.G. or just before the actual admission. The findings obtained will be discussed in detail in connection with the follow-up examination and are mentioned only briefly here.

Normal skull X-ray	95 patients
Increased digital markings	27 patients
Deep posterior fossa	24 patients
Changes in shape	19 patients
Defects including fractures	13 patients
Pronounced venous grooves	9 patients
Diastasis of sutures	7 patients
Thin cranial walls	6 patients
Calcifications	6 patients

The X-ray descriptions used are the routine for the department.

Electroencephalography: E.E.G. was carried out in 183 cases and was normal in 23. The findings were interpreted by the same few E.E.G. specialists so that uniformity of interpretation could be assured. The findings have been subdivided into large groups by the author for practical reasons.

Possible changes	28 patients
Diffuse changes	78 patients
Diffuse and focal changes	4 patients
Focal changes	50 patients

The individual changes which occurred in these groups can be seen in the case reports.

Summary of examinations performed.

P.E.G. is usually carried out as V.E.G. or S.E.G. and only in exceptional cases as L.E.G. Measurements of the ventricular system have been made by Evans' method. Furthermore, each side has been measured separately. A number of different conditions have been evaluated and the material has been divided into five major groups, bilateral dilatations with the same or different ratios on each side and with or without displacement of the ventricular system, and finally unilateral dilatations. In contrast to most reports of measurements of the ventricular system, this material is made up of almost equal numbers of symmetrical dilatations and other types.

A rise in temperature following the examination was seen in 75% of the V.E.G.'s and 60% of the S.E.G.'s. There were relatively few complications. Among 152 successful V.E.G.'s 20 developed complications and among 118 S.E.G.'s 11 developed complications but 2 patients died. It must be remembered that many of the patients included in this material were in poor general condition to begin with and there was, therefore, a greater risk that some of them would die independently of the examinations performed.

Of 186 X-ray studies 95 were normal. The changes most frequently encountered were increased digital markings in 27 cases, deep posterior fossae in 24 cases and changes in shape in 19 cases. E.E.G. was performed on 183 cases, of which 23 were normal, 82 showed diffuse dysrhythmia and 54 focal changes.

CHAPTER IV

Follow-up Examination

A: EXTENT AND METHOD OF FOLLOW-UP

In this material there is the risk that at the time of follow-up a great many of the patients will either be dead or in mental institutions. Because of this it was necessary to use an elaborate follow-up procedure which, however, had the advantage that it avoided contacting families affected in this way.

Questionnaires were sent to all admitting doctors and the response was good in most cases. The admission registers of the larger institutions for the mentally retarded were examined and information was obtained about patients under care. When it was found that the patient had moved or no reply was received from the admitting doctor, the population registers were consulted. After collection of information on those who had died, and after visiting the oligophrenic patients placed in institutions, the remaining patients were contacted. Home visits were arranged and there was excellent co-operation from the parents. Only one family did not wish to be visited but preferred that the information be obtained from the family doctor. In this connection it is of interest to note that a number of families had apparently been expecting a visit. They frequently had small problems which could be resolved by talking matters over and it would seem that some arrangement for home visiting deserves consideration.

A great many of the patients had been attending special departments, the epileptic patients frequently "Filadelfia" (the hospital for epileptics), the cerebral palsy patients the Paediatric Department at Rigshospital or the Orthopaedic Hospital in Copenhagen, and another group of patients had been attending the Neuromedical and Neurosurgical Departments after discharge.

Some of the patients came from other countries and attempts were made to trace them. In one case it was impossible to trace the patient further than France. She was a Yugoslavian girl whose family, after living in Denmark and France, emigrated to the United States. As far as the rest of these patients were concerned it was possible to obtain detailed information from the doctors who were treating them.

The main part of the follow-up was carried out between July 1956 and July 1957 but information obtained later, e.g. concerning patients who had died was also included. In a very few cases it was not possible to make

personal contact with the patients but detailed information on the course of the disease was obtained from hospitals, clinics etc.

The follow-up of the 271 patients was made up as follows:

Personally examined by the author	192
Detailed information obtained (mainly foreign patients)	19
Insufficient information obtained (one was the aforementioned Yugoslavian girl, the other a patient who had moved 12 times and is now married for the third time since discharge but failed to attend)	2
Dead at the time of follow-up	58

The follow-up examination included one or more visits to the patients and detailed discussion regarding the course of the illness and retrospective information from earlier case histories etc. In addition, detailed information was obtained about the patient's ability to adjust to school, work, marriage and all other conditions which could give a more comprehensive picture of the patient (Table 12). The follow-up included a physical examination and an assessment of the mental state.

Table 12

Educational and professional status

Too young to evaluate scholastic ability	47 (19 dead)
No information	1
At normal school	50 (1 dead)
At special school	18
for backward children	9
for mentally retarded	5
for physically handicapped	3
for the blind	1
In normal employment	41 (1 dead)
professional	4
skilled	8
unskilled	15
self-employed	3
housewives and housework	10
no information	1
In this group 8 are married. One has one healthy child. One has 2 healthy children. One has one healthy child and one child with convulsions.	
Pensioned	6
In a home for the chronic sick	2 (1 dead)
In a home for epileptics	9 (3 dead)
In a State Institution for retarded speech	1
Under State mental care	77 (28 dead)
Mentally retarded but not under care	19 (5 dead)

Total.. 271 (58 dead)

Such a follow-up could be evaluated from at least two points of view:

Firstly classification of the patient's condition at the time of follow-up, viz. healthy, handicapped slightly but not sufficiently to prevent him supporting himself, handicapped sufficiently to require hospital or institutional care, and finally, dead.

Secondly the classification could be based on the change in the patient's condition from the time of the first admission to the time of follow-up. These changes could be indicated by such terms as improved (including healthy), unchanged, worse (including dead). Furthermore it was found helpful to have two transitional groups, improved \rightarrow unchanged and unchanged \rightarrow worse.

The first classification can be considered medico-social and should be immediately acceptable as one should be in no doubt, except in a very few cases, as to which group the patient belongs. It should be mentioned that in the group of healthy patients a few are included with headaches or similar non-handicapping complaints.

The second classification is more difficult, for instance in patients with frequent convulsions at the time of admission and concomitant hemiplegia. At the time of follow-up three or four years later the hemiplegia was unchanged but the convulsions had diminished to a single one with long intervals of freedom. Such patients have been placed in the group improved \rightarrow unchanged. Included in the group improved there are a few who were admitted with severe and frequent convulsions and were at the same time imbeciles. In some of these cases the convulsions had ceased completely and the intellectual state had improved or remained unchanged. All the healthy patients were found in the improved group but the reverse was not always the case. The above-mentioned example of the imbecile patient illustrated a follow-up result which in the first classification would be placed lower on the scale than in the second. The following is an example of the opposite finding, a patient who had a slight headache and a single convulsion at the time of insufflation but who later developed a hemiplegia and more frequent convulsions with an unchanged headache. In this case the clinical condition was worse although the patient was doing well in everyday life. These comments underline the fact that even if there is good correlation between the P.E.G. findings and the two classifications, the same patients do not necessarily occur at corresponding levels of the scales.

B: RESULTS OF FOLLOW-UP EXAMINATION IN RELATION TO TYPE OF P.E.G. AND SIZE OF RATIOS

If the results obtained from the follow-up examination of the different types of P.E.G. are considered, it can be seen that they are approximately the same for the four types of bilateral ventricular dilatation and are worst in the group with displacement of the ventricular system and unequal ratios. As one

might expect, the prognosis is best in cases of unilateral dilatation because on one side there is normal distribution between the brain tissue and ventricular system (Table 13).

Table 13

Comparison between follow-up results and type of ventricular dilatation

Ventricular dilatation	Without displacement	With displacement
Bilateral with same ratio on both sides	43 healthy..... 28% 32 handicapped.. 21% 39 under care... 26%	5 healthy..... 16% 11 handicapped.. 35% 8 under care... 26%
Total 183	38 dead..... 25%	7 dead..... 23%
Bilateral with different ratios	6 healthy..... 18% 8 handicapped.. 24% 14 under care... 41%	2 healthy..... 5% 14 handicapped.. 35% 17 under care... 43%
Total 74	6 dead..... 17%	7 dead..... 18%
Unilateral with same ratio on both sides Total 4	1 healthy 1 handicapped	2 healthy
Unilateral with different ratios Total 10	2 healthy 2 handicapped	1 healthy 2 handicapped 3 under care

In the four groups with bilateral dilatation approximately 50% are healthy or only slightly handicapped, and approximately 50% are under institutional care or are dead. When the type of dilatation is ignored a comparison of the results of follow-up examination with the ratios shows a marked fall from 75% in the best groups where the ratios are small to 12% in those with the most severe degrees of dilatation (Table 14). In the group with small ratios 25% are under institutional care or are dead and the numbers rise to approximately 90% in children with a ratio of over 0.50. *The prognosis becomes worse as the ratio increases.*

Table 14

Comparison between follow-up and ratio regardless of type of dilatation

Ratio	Total	Result of follow-up			
		Healthy	Handicapped	Under care	Dead
<0.29.....	37	19 (51%)	9 (24%)	5 (14%)	4 (11%)
0.30-0.34.....	105	29 (28%)	31 (30%)	28 (27%)	17 (16%)
0.35-0.39.....	64	12 (19%)	20 (31%)	17 (27%)	15 (23%)
0.40-0.49.....	39	2 (5%)	7 (18%)	22 (56%)	8 (21%)
>0.50.....	26	0	3 (12%)	9 (35%)	14 (54%)

It seems likely that those patients with small ratios who were found to be healthy at the time of follow-up were the same patients who had minimal symptoms on admission. The same considerations have been applied to the second follow-up classification and identical results have been obtained (Table 15).

Table 15
P.E.G. and clinical changes

Type of ventricular dilatation	Ratio	No.	Improved	Unchanged to improved	Unchanged	Unchanged to worse	Worse *
Bilateral, same ratio no displacement	≤ 0.29	21	13	1	2	0	5 (4)
	0.30-0.34	63	31	5	6	3	18 (14)
	0.35-0.39	41	13	4	7	2	15 (11)
	0.40-0.49	17	2	1	4	1	9 (3)
	≥ 0.50	10	0	0	0	1	9 (6)
Bilateral, same ratio with displacement	≤ 0.29	0	0	0	0	0	0
	0.30-0.34	17	8	1	2	2	4 (3)
	0.35-0.39	8	1	1	0	1	5 (2)
	0.40-0.49	3	1	0	1	0	1 (0)
	≥ 0.50	3	1	0	0	0	2 (2)
Unilateral, same ratio	≤ 0.29	4	3	0	1	0	0
Unilateral, diff. ratio	≤ 0.29	8	3	1	1	1	2
	0.30-0.34	1	1	0	0	0	0
	0.35-0.39	1	0	0	0	1	0
Bilateral, diff. ratio no displacement	≤ 0.29	3	2	0	1	0	0
	0.30-0.34	10	3	3	1	1	2
	0.35-0.39	8	2	1	2	1	2 (2)
	0.40-0.49	10	0	0	2	4	4 (2)
	≥ 0.50	3	0	0	0	0	3 (2)
Bilateral, diff. ratio with displacement	≤ 0.29	1	0	0	1	0	0
	0.30-0.34	14	3	2	3	5	1
	0.35-0.39	6	2	1	2	0	1
	0.40-0.49	9	0	1	2	1	5 (3)
	≥ 0.50	10	1	1	0	1	7 (4)

* The number of fatal cases included in the first figure is indicated by the figure in brackets.

In Table 16 the change in clinical condition is recorded with reference to the ratio, and this can be compared with Table 14. 80% with a ratio of less than 0.30 have been placed in the unchanged or improved groups. Even if it is not the same patients who are placed in the unchanged to improved groups or the handicapped to healthy groups, the relative distribution is the same regardless of the classification, and thus an increasing dilatation indicates a worse prognosis.

Table 16

Changes in the clinical condition in relation to ratio, regardless of type of dilatation

Ratio	Total	Improved	Unchanged to improved	Unchanged	Unchanged to worse	Worse*
≤ 0.29.....	37	21 (59%)	2 (5%)	6 (16%)	1 (3%)	7 (19%) (4)
0.30-0.34....	105	46 (44%)	11 (10%)	12 (11%)	11 (10%)	25 (24%) (17)
0.35-0.39....	64	18 (28%)	7 (11%)	11 (17%)	5 (8%)	23 (36%) (15)
0.40-0.49....	39	3 (8%)	2 (5%)	9 (23%)	6 (15%)	19 (49%) (8)
≥ 0.50	26	2 (8%)	1 (4%)	0	2 (8%)	21 (81%) (14)
	271	90	23	38	25	95 (58)

* The number of fatal cases included in the first figure is indicated by the second figure in brackets.

C: EVANS' RATIO COMPARED WITH SCHIERSMANN'S INDEX

Schiersmann (p. 52) suggested an index at the same time as Evans proposed his ratio. His index is calculated by dividing the greatest external cranial width by the greatest width of the cella media (Fig. 1). As previously stated, this index has been used in a number of European reports (*Brenner, Schönenberg and Ott, Heidrich, Kohler, Krischek, Vinken et al., Bruijn*), and has been applied to the present material (Table 17). The results obtained by this method show that small indices corresponding to severely dilated ventricles comprise 8% of the healthy to handicapped group whereas an index above 4.0 corresponding to a normal ventricular system comprises 75% of the children in the two best groups.

As previously stated in the discussion of methods of measurement, these two systems correspond to one another.

It would appear to be of value to compare these systems, and it has been possible to obtain comparable measurements on 231 examinations carried out on 222 patients. Of particular interest is the way the two values correspond to the results of the follow-up examination, and this can be seen from Fig.

Table 17

Schiersmann's Index and follow-up results

Index	No.	Healthy	Handicapped	Under care	Dead
Below 2.0.....	2	0	0	2 (100%)	0
2.0-2.9.....	37	0	3 (8%)	25 (68%)	9 (24%)
3.0-3.4.....	56	11 (20%)	20 (36%)	13 (23%)	12 (21%)
3.5-3.9.....	67	13 (19%)	17 (25%)	23 (34%)	14 (21%)
4.0-4.4.....	45	17 (38%)	15 (33%)	8 (18%)	5 (11%)
4.5-5.1.....	24	14 (58%)	6 (25%)	2 (8%)	2 (8%)

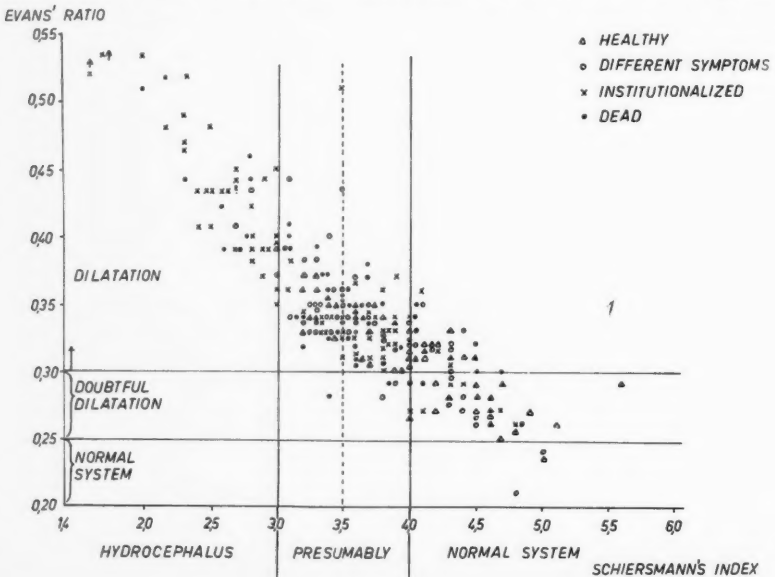
24 where Schiersmann's index is used as abscissa and Evans' ratio as ordinate. From this it may be seen that there is a close relationship between the two values. With an index less than 3.0 the prognosis is poor and there are no healthy patients. This is comparable to the ratio of 0.40 and above. An index of 4.0 and above, corresponding to a normal system, comprises some handicapped patients and few deaths. From Fig. 24 it may be seen that a great many of the patients examined with a ratio of 0.25-0.35 are doing well and, as suggested by Göllnitz, one must consider raising the upper limit of normal for the ventricular system in children.

The ventricular systems which cannot be measured by Schiersmann's method are the most asymmetrical and dilated systems. This is indicated indirectly by *Vinken et al.* who require a symmetrical system before attempting to measure it and by *Schiersmann* in the latest edition of his textbook. He gives examples of measurements and at the same time describes five children with cerebral palsy in whom measurement was not attempted. His illustration of the measuring methods has changed and is now even more comparable with the methods suggested by Evans.

No definite conclusion can be drawn from the present material because it was selected with special reference to Evans' ratio but it would seem that the two measuring methods on the whole give the same results, and that the index is no easier to measure than the ratio; in fact, it is more difficult to use when the ventricular systems are asymmetrical and severely dilated.

Fig. 24

A comparison of Evans' ratio and Schiersmann's index in relation to the follow-up result.



D: DISPLACEMENT OF THE VENTRICULAR SYSTEM IN RELATION TO THE FOLLOW-UP EXAMINATION

In addition to measuring the degree of dilatation of the lateral ventricles, a number of other changes are recorded in each P.E.G. (p. 73). Displacement of the ventricular system to one side has been discussed several times in the literature. *Crothers et al.* consider displacement as an indication of atrophy on the side to which the displacement occurs, and in the present material where tumours are excluded, this is usually the case. Nevertheless, there are space-occupying lesions which are not tumours, e.g. cysts, porencephalies, subdural haematomas and hygromas. In such cases one would expect the displacement to be away from the affected side. The extent to which the ventricular system can be displaced without being abnormal has been discussed. *Eaglesham* has pointed out the possibility that a slight displacement could be due to the septum pellucidum bulging to one side or the other, and this can especially be seen in those cases where the head is directed to one side for temporal horn filling.

Robertson and Childe showed that "normal displacements" of the ventricular midline were less than 0.5 mm. (This is a displacement compared to a fixed midline and not the difference between distances as in the present report but approximately half of this).

Eek et al. require 2 mm. displacement before considering the ventricular system displaced. In the present material 5 mm. displacement is required before it is considered abnormal. This has the advantage that it takes into consideration both the above-mentioned "normal displacements" as well as possible errors in measurement, as mentioned on p. 72, which could influence the difference by 2 mm. Atrophy of a hemisphere is the most likely cause of displacement of the ventricular system and the importance of the degree of displacement in relation to the prognosis has been examined, as a marked displacement would suggest a severe loss of brain substance on one side.

Table 18 shows the displacement of the ventricular system in 77 patients. In 48 patients it was 5-9 mm., in 19 patients 10-14 mm. and in 10 patients 15 mm. or more. The table shows the results of follow-up examination in each of the three groups and it is shown that with the smallest displacement 50% are under institutional care or are dead. In the group with 10-14 mm. displacement the figures are approximately the same whereas in the group with the most severe displacement there is one healthy patient, 3 with borderline intelligence, 4 with normal intelligence but with other handicaps, and only 2 with severe mental retardation. In the three groups the distribution of displacement to the right and the left side is the same. The two complaints most commonly encountered in all three groups are hemiplegia and epilepsy. Of the 77 patients 24 had hemiplegia and 36 epilepsy. The greatest degrees of displacement are usually seen in cases with unequal ventricular dilatation.

Table 18

Displacement of ventricular system in relation to follow-up results

	Degree of displacement		
	5-9 mm.	10-14 mm.	≥ 15 mm.
Total.....	48	19	10
No. in which displacement was to the left	24	8	5
Healthy.....	8	1	1
Inferioritas intellectualis (I.Q. > 75)....	8	4	3
Debilitas mentis (I.Q. 55-75).....	6	4	1
Imbecilitas (I.Q. 35-55).....	6	1	1
Idiotia (I.Q. < 35).....	7	0	0
Fatal cases.....	7	7	0
Normal I.Q. with hemiplegia, epilepsy or other conditions.....	6	2	4
Total with hemiplegia.....	10	8	6
Total with epilepsy.....	23	7	6

Eight patients with displacement of 15 mm. or more have unequal ratios whereas only 2 have an equal ratio on the two sides.

Five patients (cases no. 197, 250, 261, 269 (Fig. 16), 270, (Fig. 17)) have a displacement contrary to that expected from the clinical picture showing ventricular displacement to the same side as a hemiplegia. It can be seen that these patients form a special group. One patient was operated on for a cyst causing severe convulsions. Two of the children were later hemispherectomised because of uncontrollable seizures and psychological changes. In both patients severe changes were found accompanied by a large amount of fluid. One is tempted to consider diagnostic craniotomy in these cases, and *Biernond* (1958) is of the same opinion as regards neurosurgical exploration in cases of hemiplegia which show atypical findings. In these cases failure of the pyramidal tract to cross must be considered.

E: VENTRICULAR DILATATION WITH UNEQUAL RATIOS IN RELATION TO THE FOLLOW-UP EXAMINATION

It has been stated in the discussion on measuring methods that a possible error of 1 mm. may change the ratio 0.01 if the error concerns the width of the anterior horns. This would make a ratio difference of 0.02 at the most, depending on the measuring method. If the measurement of the anterior horns as well as the cranial diameter were wrong, and these errors did not compensate one another, the total error would be 0.02-0.03. *Göllnitz* measured each lateral ventricle separately and he felt that if the difference was greater than 0.04 the system was asymmetrical. It seems reasonable to use 0.05 as the upper limit of normal.

Table 19

Ventricular dilatation with unequal ratios in relation to follow-up results

	Ratio difference			
	0.06-0.09	0.10-0.14	0.15-0.19	0.20→
<i>1. Ventricular system without displacement</i>				
Healthy.....	6	-	-	-
Normal I.Q. with miscellaneous symptoms.....	4	-	-	-
Inferioritas intellectualis (I.Q. > 75)..<	4	-	-	-
Debilitas mentis (I.Q. 55-75).....	2	-	1	-
Imbecilitas (I.Q. 35-55).....	3	3	1	1
Idiotia (I.Q. < 35).....	1	2	-	-
Fatal cases.....	2	4	-	-
<i>2. Ventricular system with displacement</i>				
Healthy.....	3	-	-	-
Normal I.Q. with miscellaneous symptoms.....	3	2	-	2
Inferioritas intellectualis (I.Q. > 75)..<	4	2	1	-
Debilitas mentis (I.Q. 55-75).....	3	-	4	-
Imbecilitas (I.Q. 35-55).....	2	-	-	1
Idiotia (I.Q. < 35).....	1	1	1	1
Fatal cases.....	4	2	-	2

It has been mentioned earlier that displacement of the ventricular system can result in a difference in the ratios even if the lateral ventricles are the same size. This is due to the fact that brain tissue as well as the ventricular system is being measured, and this distribution can be different on the two sides.

Table 19 shows ratio differences of more than 0.05, and at the same time indicates the displacement of the ventricular system. The size of the difference has been examined with regard to prognosis in the following sub-groups: 0.06-0.09, 0.10-0.14, 0.15-0.19 and 0.20 and over. It can be seen that with increasing differences and increasing ratios prognosis becomes worse regardless of the displacement of the system. Thirty-four patients have a ratio difference above 0.05 and no displacement of the system. Of these 6 were healthy at the time of follow-up. The group with displacement of the ventricular system includes 40 patients of whom 3 were healthy at the time of follow-up. The above-mentioned considerations also apply to cases with bilateral changes. The small group with unilateral ventricular dilatation consists of 10 patients with ratio differences above 0.05 and 7 of these have ventricular displacement. The prognosis in this group is, on the whole, good. Two patients have displaced systems without any ratio differences. The patient with the greatest degree of displacement is well, the other has a minor intellectual handicap, hemiplegia and epilepsy.

F: PROGNOSTIC VALUE OF CORTICAL AIR

As mentioned earlier, the value of cortical air findings in the present work is based on certain criteria. The air must be in the same position in several pictures and the changes of such a size that there is no doubt that the sulci are widened. Exact figures are not used and *Schnitker and Ulrich* reported that an attempt to calculate an index was unsuccessful. The cortical changes are assessed on the same pictures as the ventricular dilatations where a requirement had been a well-filled system; in addition, these assessments are made on the immediate pictures and not the twenty-four hour photographs. The use of these pictures is based on the hypothesis that the sub-arachnoid space can be altered according to the amount of air placed in it, and the same is true of the twenty-four hour pictures of the ventricular system. (*Troland, Baxter and Schatzki; Jirout; Paul and Erickson*).

If one considers the possibility of large amounts of air entering the sub-arachnoid space instead of the ventricular system, it is reasonable to assess the cortical changes on the same pictures as those on which one would measure the ventricular system. Occasionally one finds evidence of severe sub-arachnoid changes when the ventricular system is not well-filled and these changes cannot be found again when the ventricular system is well-filled (Figs. 25, 26). Cortical changes are classified as generalised, unilateral and localised. The localised changes fall mainly into two groups: (a) frontally placed and (b) localised to the Sylvian fissure and the insular area.

Twenty-three children showed bilateral cortical changes and at the time of follow-up none was normal, 6 were handicapped, 7 under institutional care and 10 dead.

Seven children had unilateral changes and at follow-up one was normal, one handicapped, 2 under institutional care and 3 dead.

Localised changes were found in 18 children, of whom 2 were normal at follow-up, 4 handicapped, 6 under institutional care and 6 dead.

Of 48 children with abnormal amounts of cortical air 19 were dead at the time of follow-up (there were 58 deaths in the whole material), 15 were under institutional care (94 in the whole material), 11 handicapped (70 in the whole material), and only 3 were normal (62 in the whole material). *This shows that an abnormal amount of cortical air, independent of type, is a serious prognostic sign, but the presence of generalised cortical air is the most serious.*

Table 20 shows cortical air in relation to changes in clinical condition and gives the same results as those seen above.

Cortical findings are compared with the types of ventricular dilatation (Table 21). Of 152 patients with bilateral dilatation without displacement and with the same ratio on both sides, 13 of the 38 who died had cortical changes. One may think that the serious prognostic significance of cortical air alone could be explained by its association with large ratios. This is not the case,

Table 20

Cortical air changes in relation to changes in clinical condition

	Generalised changes	Unilateral changes	Localised changes
Total.....	23	7	18
Improved.....	1	1	4
Unchanged to improved.....	3	1	0
Unchanged.....	4	1	3
Unchanged to worse.....	2	0	2
Worse (no. dead).....	13 (10)	4 (3)	9 (6)

Table 21

Type of P.E.G. and cortical air findings related to the follow-up results

	Without displacement of ventricular system			With displacement of ventricular system		
		Without abnormal cortical air	With abnormal cortical air		Without abnormal cortical air	With abnormal cortical air
Bilateral ventricular dilatation with same ratio on each side 183	healthy.....	42	1	healthy.....	5	0
	handicapped.	26	6	handicapped.	7	4
	under care...	31	8	under care...	7	1
	dead.....	25	13	dead.....	6	1
Bilateral ventricular dilatation with different ratios on each side 74	healthy.....	4	2	healthy.....	2	0
	handicapped.	7	1	handicapped.	14	0
	under care...	12	2	under care...	13	4
	dead.....	3	3	dead.....	5	2

however. On the contrary, only a few patients with ratios of 0.50 or more showed any cortical changes. This could be due to the difficulty of getting air into the sub-arachnoid space especially in children with a severe degree of dilatation and to the fact that air is more easily kept in a severely dilated system.

The distribution of the findings of cortical changes in the different groups of follow-up results can be seen from the table and, as expected, the findings are mainly among those patients who have a poor prognosis.

Among the localised cortical changes there are two which are found in a number of cases. Frontally placed air is seen in 19 patients in 9 of whom it is combined with other forms of cortical air. Of the 10 children who had only a frontal air collection, one was healthy at the time of follow-up, 2 were handicapped, 3 under institutional care and 4 had died. The patient who had done

best was a child who was 6 years old at the time of P.E.G. Among the children below one year of age 2 were handicapped, 2 under institutional care and 2 had died. Of 9 children with frontal air combined with other cortical changes, 3 were handicapped, 3 under institutional care and 3 had died at the time of follow-up. The finding was most often seen in combination with bilateral cortical air (7 patients) but in 2 the cortical air was unilateral.

Of 19 patients 7 were below the age of two at the time localised air collections were demonstrated. The prognosis for these patients is better than for the patients with other types of cortical changes and must be considered with some reservation.

The other localised finding is air corresponding to the Sylvian fissure and the insula area. This was found in 8 children, (cases no. 18, 59, 74, 98, 122, 154, 200, 215).

This finding can be divided into two groups, one where changes are bilateral (3 patients) and the other where they are unilateral (5 patients). In the first group two were dead at the time of follow-up; a third child was well and was in a nursery home showing signs of slight mental retardation and was a "non-talker and non-jumper," (*Plum 1955*).

The 5 children with unilateral localised changes were made up of 2 healthy children at the time of follow-up, one handicapped, one with a severe handicap who should have been under institutional care and one dead. Altogether, 2 of the 8 were healthy, 2 slightly handicapped, one who should have been under institutional care and 3 dead.

The presence of sub-dural air in large amounts was seen in 9 patients (cases no. 83, 99, 137, 138, 147, 193, 214, 230, 231) i.e. 3% of those examined. Seven had had V.E.G. and 2 S.E.G. Five of the changes were right-sided and one left-sided. One was bilateral and one localised to the temporal poles, and finally one had sub-dural air infra-tentorially.

At the time of follow-up 3 patients had died, 3 were severely mentally retarded (2 of these had, in addition, cerebral palsy), 3 had a normal I.Q. but two had epilepsy and one hemiplegia. Only one had no symptoms apart from bad temper. In this case the sub-dural air was localised solely to the right occipital region.

There has been a great deal of discussion on the mechanism of this air, and many authors support the idea that it is due to an error in the position of the syringe but this is chiefly true of L.E.G., (*Smith and Crothers*). Another possibility is a rupture between the sub-arachnoid and sub-dural spaces (*Paul and Erickson, Howard*). The significance of this finding has been discussed and *Lemerc and Barnacle* found a higher mortality in cases with sub-dural air in their 800 examinations. *Boudreau and Crosby* maintain that the presence of air in the sub-dural space in large amounts almost invariably indicates fluid in this space, and consider further investigation justified. The existence of

sub-dural air of any kind or amount in their material of 159 children below the age of two years was 41%.

Similar findings cannot be demonstrated in the present material. One patient was operated on and a large arachnoid cyst perforating the septum pellucidum was found.

G: THE PRESENCE OF PORENCEPHALIES AND MID-LINE ABNORMALITIES IN RELATION TO THE FOLLOW-UP RESULTS

P.E.G. revealed porencephalies in 5 cases (cases no. 8, 84, 101, 159, 220) of which 2 were dead, 2 were idiots and one had hemiplegia at the time of follow-up. These were communicating porencephalies, and autopsy later showed a further 3 to have non-communicating porencephalies.

Mid-line abnormalities were found in 7 patients with cysts of the septum pellucidum, one had a Verga cyst and one had agenesis of the corpus callosum. Of the 7 patients with cysts of the septum pellucidum (cases no. 48, 64, 98, 110, 128, 138, 271) one was healthy at the time of follow-up, 2 mentally retarded (one of the latter had, in addition, epilepsy and the other was a "non-talker, non-jumper"), 2 were severely mentally retarded and had spastic tetraplegia, and 2 were dead.

The patient with a Verga cyst was mentally retarded, had microcephaly and convulsions (case no. 136).

The patient with agenesis of the corpus callosum (case no. 11) had died. The small figures in this group do not allow any conclusions to be drawn concerning the prognostic value of the abnormalities but it seems very doubtful whether one can completely ignore the presence of such malformations and merely state that, by themselves, they are of no significance.

H: THE WIDTH OF THE THIRD VENTRICLE IN RELATION TO THE FOLLOW-UP RESULTS

The width of the third ventricle measured in the AP projection has in the last few years been subject to a great deal of discussion concerning its prognostic value in adults. *Engeset and Lønnum* (1958) showed that a widened third ventricle had serious prognostic implications. In the discussion on the measuring methods the exact figure for the third ventricle's width is mentioned, and this varies from 2-8 mm., averaging about 5 mm. (*Davidoff and Dyke* 1937; *Schiersmann* 1942; *Göllnitz* 1951; *Nürnberg and Schaltenbrand* 1955; *Robertson* 1957).

Göllnitz (1954) gives some measurements of the third ventricle in children with psychiatric disorders, and to some extent these figures can be considered as normal values for the age group six to fourteen years. *Durand and Scagliotti* (1951) give some figures for infants.

Nürnberg and Schaltenbrand give the correlation between the width of

the third ventricle and the cranial diameter in adults. *Eek* states that a normal third ventricle in children should not be wider than 6 mm. An isolated attempt has been made to produce an index for the area of the third ventricle in relation to the lateral ventricles (*Schiffer* 1951).

It has been possible to measure the width of the third ventricle in 235 of the author's 271 cases, and the values can be seen on p. 76. These figures are related to age (Fig. 27) and cranial width (Fig. 28). From Fig. 27 it can be seen that the patients found to be healthy at the time of follow-up mostly had third ventricle widths of between 2 and 6 mm. with a corresponding increase in age. A few of the healthy children had considerably larger third ventricles but these were often patients with random seizures and without any kind of handicap and they were seen in the very early age group. The children who later had minor handicaps were found particularly in the younger age group with wider third ventricles than those in the healthy groups. But in the older age groups this difference disappears. The greatest deviation can be seen in the prognostically worse groups where we find a considerable number of large third ventricles compared with the two better groups, and this is the same in all age groups.

Compared with cranial diameter it can be seen that the healthy children are found within rather narrow limits, i.e. 14-16.5 cm. cranial width and showing third ventricles of 2-6 mm. Compared with corresponding figures from the adult group reported by *Nürnberg* and *Schaltenbrand* there are more children with small ventricles than in the adult group. The children with slight handicaps are to be found in the neighbourhood of the normal group, very often having too small a cranial width and too wide a third ventricle. As far as the children under institutional care and those who had died are concerned, the difference is much more pronounced and here we find particularly wide third ventricles.

As age and cranial width can play a major part, these two values have been used as ordinate and abscissa and the third ventricle as well as the result of the follow-up has been placed within this system (Figs. 29, 30, 31, 32). From these it can be seen that the healthy children are placed close to or above the normal curve obtained from *Meredith's* figures. In contrast no patients with small cranial diameters have done well, which corresponds to the prognostic significance of microcephaly, (p. 118). If the cranial width is above normal the size of the third ventricle seems to influence the course.

Finally, the correlation between ventricular ratio and the width of the third ventricle has been examined and in Fig. 33 it can be seen that a large third ventricle frequently accompanies a severely dilated system. Where this is not the case a third ventricle of more than 8 mm. is a sinister prognostic sign and perhaps the most important single figure.

Fig. 27.

Width of the third ventricle and age in relation to follow-up examination.

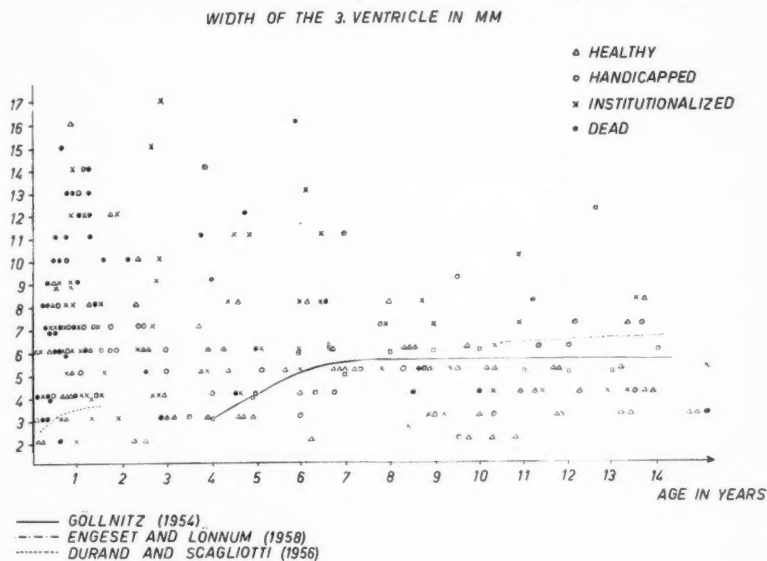


Fig. 28.

Width of the third ventricle and internal width of the cranium in relation to the follow-up result.

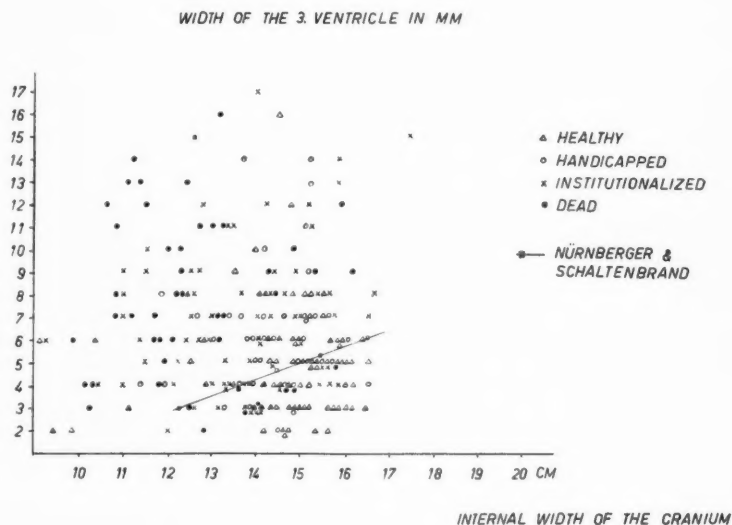


Fig. 29.

Curve: Meredith's normal values (1953). Width of the third ventricle related to the internal width of the cranium and to age in the group found to be healthy at follow-up.

HEALTHY.

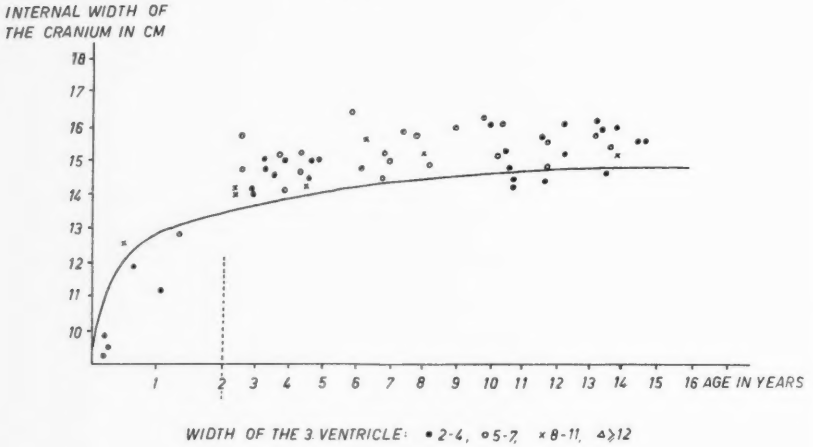


Fig. 30.

Curve: Meredith's normal values (1953). Width of the third ventricle related to the internal width of the cranium and to age in the group found to be healthy at follow-up.

HANDICAPPED

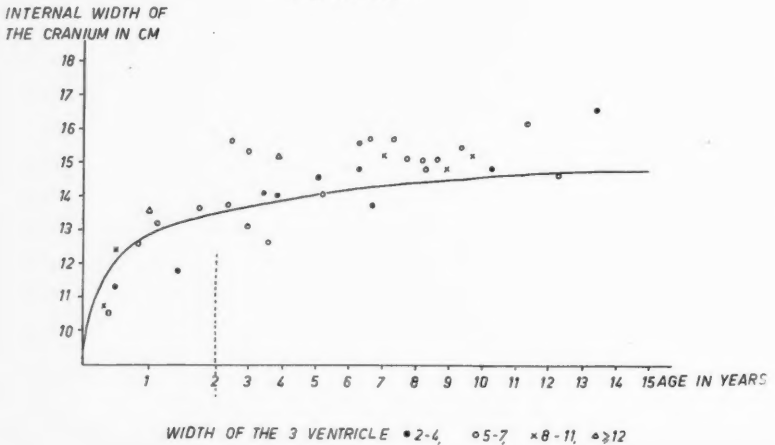


Fig. 31.

Curve: Meredith's normal values (1953). Width of the third ventricle related to the internal width of the cranium and to age in the group found to be institutionalised at follow-up.

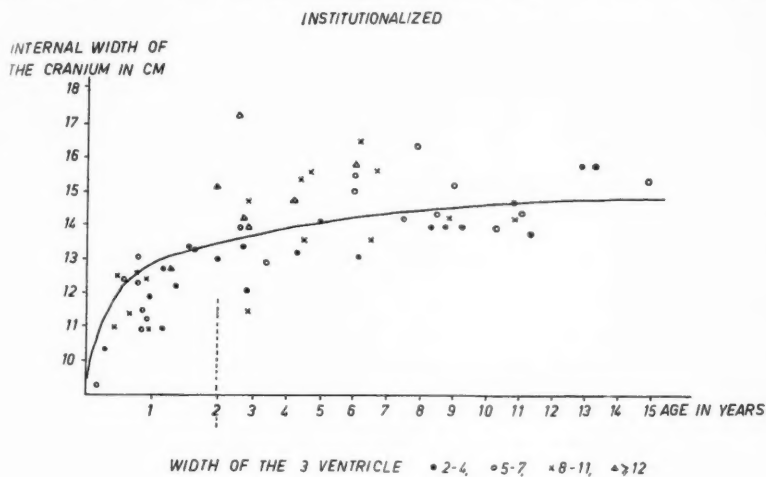


Fig. 32.

Curve: Meredith's normal values (1953). Width of the third ventricle related to the internal width of the cranium and to age in the group found to be dead at follow-up.

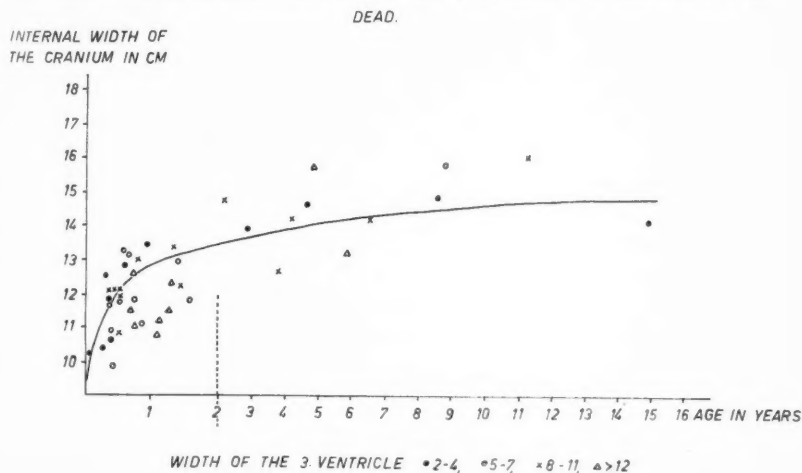


Fig. 33.

Width of the third ventricle related to ventricular ratio and follow-up result.

WIDTH OF THE 3. VENTRICLE

VENTRICULAR RATIO	2-4 MM	5-7 MM	8-10 MM	≥ 11
≤ 0,29	▲▲▲▲▲▲▲▲ ▲▲ ○○○○	▲▲▲▲ ○○○○○○ x ●	●	●
0,30-0,39	▲▲▲▲▲▲▲▲ ▲▲▲▲ ○○○○○○○○ ○○ ●●●●●●●● x x x x x x x x ●●●●●●●●	▲▲▲▲▲▲▲▲ ▲▲ ○○○○○○○○ ○○○○○○ ●●●●●●●● x x x x x x x x ●●●●●●●●	▲▲▲▲▲ ○○○○○○ ○○○○○○ x x x x x x x x ●●●●●●●●	▲ ○○ x x x x x ●●●●●
0,40-0,49	x x	▲ ○○○ x x x x x ●●●	x x x x x ●●●	○ x x x x ●●
≥ 0,50	x ●	○ x	x ●	○○ x ●●●

▲ HEALTHY x UNDER CARE
 ○ HANDICAPPED ● DEAD

I: THE PERIOD OF OBSERVATION IN RELATION TO THE FOLLOW-UP RESULTS

The influence of a number of previously mentioned factors on the P.E.G. and prognosis was examined, but before this can be discussed the length of the observation period has to be considered. A one year period of observation has been suggested for the patients in the present material. From Table 22 it can be seen that the group with an observation period of less than one year consisted entirely of children who died before the follow-up began with the exception of one foreign child who could not be traced. After the first year there is not much difference when compared with the change in the clinical condition. That a short period of observation should lead to a relatively higher number of improved or unchanged patients, which one might expect, bearing in mind that the eventual progression of symptoms would be slow and not become manifest for several years, has not been seen.

J: SEX AND AGE AT THE TIME OF ADMISSION IN RELATION TO P.E.G. FINDINGS

The age at the time of admission to the Neurosurgical Department has been tabled earlier (p. 62). It was possible that a certain type of P.E.G. change was related to a particular age group but this is shown not to be the case and the distribution is fairly uniform over the years, (Table 23). The only

Table 22

Period of observation in relation to changes in clinical condition

Period of observation	No. of pts.	Improved	Improved to unchanged	Unchanged	Unchanged to worse	Worse	No. dead
< 1 year ...	28	0	0	1	0	27	27
1-2 years....	18	5	0	2	0	11	11
2-3 -	29	6	1	7	2	13	7
3-4 -	17	6	2	5	0	4	3
4-5 -	21	5	3	2	3	8	4
5-6 -	26	13	2	1	3	7	2
6-7 -	20	7	3	1	4	5	1
7-8 -	19	7	3	5	3	1	0
8-9 -	28	10	4	3	3	8	2
9-10 -	19	11	1	5	2	0	0
10-15 -	26	13	2	3	4	4	0
15-20 -	18	7	2	2	3	4	1
20-25 -	2	0	0	1	0	1	0
	271						58

Table 23

Sex and age on admission in relation to different types of ventricular dilatation

Age on admission	Total	Bilateral dilatation with same ratio on each side		Unilateral dilatation	Bilateral dilatation with different ratios	
		without displacement	with displacement		without displacement	with displacement
0-11 mths.....	74	47	11	1	9	6
1-2 yrs. 11 mths.....	63	28	8	1	13	13
3-7 yrs. 11 mths.....	65	37	5	7	6	10
8-14 yrs. 11 mths.....	69	40	7	5	6	11
	271	152	31	14	34	40
Boys.....	171	102	19	7	21	22
Girls.....	100	50	12	7	13	18

exception was unilateral dilatation which was found mainly in older children, and this could be due to the fact that it is often acquired after birth. The distribution of the types of P.E.G. compared with the sex show that the bilateral changes with no ratio difference and no displacement have a distribution almost as expected except for a slight predominance of males, whereas the other forms of dilatation show a predominance of females. The figures in these groups are, however, small.

In addition to a possible correlation between a certain age group, there

Table 24

Ratio in relation to sex and age on admission

Age	Total	Ratio				
		≤ 0.29	0.30-0.34	0.35-0.39	0.40-0.49	≥ 0.50
0- $\frac{1}{2}$ year	50	8	18	10	9	5
$\frac{1}{2}$ - 2 years.....	66	2	19	16	18	11
2- 5 -	53	6	22	13	5	7
5-10 -	56	10	25	15	5	1
10-15 -	46	11	21	10	2	2
Boys.....	171	23	62	45	26	15
Girls.....	100	14	43	19	13	11

could be a correlation between the degree of dilatation, as measured by ratio, and a certain age. This correlation can be seen from Table 24 which shows that over the years there is a marked tendency for the higher ratios to disappear so that the number of children with a ratio of 0.50 or more in the age group below two years is 16, and from 2-10 years is 8. For the ratio 0.40-0.49 the figures for the same two age groups are 27 and 10 respectively.

Again we have to remember that a great many of the older children have postnatally acquired conditions. A possible explanation is that only in younger children can disturbances lead to very high degrees of dilatation. When the child is over two years of age the C.N.S. has become so resistant to disturbances that it is almost impossible to produce gross dilatation. In the same way the question of sex-linked changes has been examined, and in the group with ratios of 0.35-0.39 one finds the greatest difference between boys and girls (45/19), but this difference becomes less and less with larger ratios, and for the group 0.50 or more it is 15/11.

K: THE AGE AND TIME OF RECOGNITION OF THE DISEASE IN RELATION TO THE P.E.G. FINDINGS

In Table 25 the time of recognition of the disease is correlated to P.E.G. findings. This shows exactly the same result with regard to age as previously mentioned, so that the older the child is when the disease is recognised, the fewer severe dilatations are found. A ratio of 0.50 or more was found in only one child in whom the disease was recognised after the age of one year. There seems to be no specific change in the type of dilatation with later recognition of the disease. For both of these examinations, changes of age and P.E.G. changes, it seems that the more severe degrees of dilatation are found in younger patients. There appears to be no great difference in the type of P.E.G. with increasing age except for a slight tendency to a greater number of unilateral dilatations and greater ratio differences and displacements of the

Table 25

Age at time of recognition of disease in relation to P.E.G. findings

Disease recognised	Ratio	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios		Total
		without displacement	with displacement		without displacement	with displacement	
1st 24 hrs.	≤ 0.29.....	1	0	1	1	0	
	0.30-0.34.....	17	3	1	4	4	
	0.35-0.39.....	5	0	1	0	0	
	0.40-0.49.....	8	2	0	5	2	
	≥ 0.50.....	2	2	0	1	6	
		33	7	3	11	12	66
24 hrs.- 6 months	≤ 0.29.....	5	0	1	1	0	
	0.30-0.34.....	11	5	0	1	1	
	0.35-0.39.....	10	0	0	3	1	
	0.40-0.49.....	4	0	0	5	3	
	≥ 0.50.....	3	0	0	2	3	
		33	5	1	12	8	59
6 months- 2 years 11 months	≤ 0.29.....	1	0	3	2	1	
	0.30-0.34.....	11	7	0	2	7	
	0.35-0.39.....	13	2	0	2	3	
	0.40-0.49.....	4	1	0	1	2	
	≥ 0.50.....	4	1	0	0	1	
		33	11	3	7	14	68
3-13 years 11 months	≤ 0.29.....	11	0	5	1	1	
	0.30-0.34.....	23	2	1	1	1	
	0.35-0.39.....	11	4	0	3	2	
	0.40-0.49.....	1	0	0	0	1	
	≥ 0.50.....	0	0	0	0	1	
		46	6	6	5	6	69
No information	≤ 0.29.....	3	0	1	0	0	
	0.30-0.34.....	1	1	0	0	0	
	0.35-0.39.....	2	0	0	0	0	
	0.40-0.49.....	0	0	0	0	0	
	≥ 0.50.....	1	0	0	0	0	
		7	1	1	0	0	9

ventricular system with a higher age. After observing the correlation between younger patients and more serious degrees of dilatation, it is not surprising that by examining the time of recognition of the disease, one finds a better prognosis for the disorders which are recognised late. The poorest prognosis is among those children whose disease is recognised within the first twenty-four hours of life. The same is true, to a lesser degree, of children in whom the disorder is recognised within the first two years. After this the picture changes and for the quarter of the whole material where the disorder was recognised after the age of 3 the prognosis is much better, and only 17% are placed in the two most serious prognostic groups, whereas the rest are mainly placed in the healthy group or at least with only slight handicaps (Table 26 and Fig. 34).

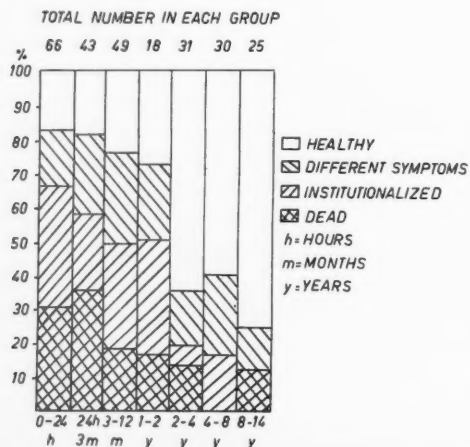
Table 26

Age at time of recognition of disease in relation to follow-up results

Symptoms	Total	Healthy	Handicapped	Under care	Dead
≤24 hrs.....	66	11	11	24	20
24 hrs.-3 mths.....	43	8	10	10	15
3-12 mths.....	49	11	14	15	9
1-1 yr. 11 mths.....	18	5	4	6	3
2-3 yrs. 11 mths.....	31	20	5	2	4
4-7 yrs. 11 mths.....	30	18	7	5	0
8-13 yrs. 11 mths.....	25	19	3	0	3

Fig. 34.

AGE AT ONSET OF SYMPTOMS
COMPARED WITH THE FOLLOW UP RESULTS



L: THE RELATION OF SYMPTOMS AND SIGNS TO THE P.E.G. AND FOLLOW-UP EXAMINATION

The symptoms found among the 271 patients have been recorded on p. 62. They fall mainly into three groups: motor handicap, epilepsy and mental retardation.

Table 27 shows the P.E.G. findings with the different forms of motor handicap, either cerebral palsy or motor retardation. Only the hemiplegic group does not conform in that this condition is most often present with an asymmetrical ventricular system. Of the 57 patients with hemiplegia 14 have bilateral dilatations with the same ratio on each side and no displacement of the system. The remaining 43 belong to the other four types of P.E.G. The majority of the 27 patients in the tetraplegic group as well as most of the remaining motor handicapped patients have bilateral dilatation with equal ratios and no displacement.

Table 27
Motor symptoms in relation to P.E.G. findings

Motor symptoms	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios	
	without displacement	with displacement		without displacement	with displacement
Spastic hemiplegia.....	2	—	1	—	2
— paraplegia.....	—	—	—	1	—
— tetraplegia.....	—	—	—	—	1
Rigidity.....	4	1	—	—	—
Flaccidity.....	1	—	1	—	—
Athetosis.....	—	—	—	—	2
Motor retardation.....	1	—	—	—	—
Spastic hemiplegia combined with other symptoms.....	12	7	5	10	18
Spastic tetraplegia combined with other symptoms.....	16	1	0	4	5
Other motor symptoms combined with other symptoms.....	49	11	0	10	2
	77	19	5	24	25

Convulsions were found in 180 of the 271 patients (Table 28), and existed as the only symptom in 46 cases. There is no particular difference in the frequency of the various types of P.E.G. combined with the different forms of seizures. In particular there is not a high incidence of asymmetrical systems in patients with focal seizures or unilateral convulsions. Again the majority show symmetrical bilateral dilatation.

Mentally retarded children (Table 29) belong to this P.E.G. group except

Table 28
Convulsions in relation to P.E.G. findings

	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios	
	without displacement	with displacement		without displacement	with displacement
Grand mal.....	14	1	1	1	2
Petit mal.....	2	0	0	1	0
Grand + petit mal.....	2	1	0	1	0
Unilateral convulsions.....	5	0	0	2	2
Focal seizures.....	1	0	1	0	0
Combined (all + unilateral).....	2	3	0	2	0
Atypical seizures.....	0	1	0	0	1
	26	6	2	7	5
All forms of seizures combined with:					
1) motor handicap.....	19	8	2	6	10
2) mental retardation.....	11	2	1	1	1
3) motor handicap and mental retardation.....	32	6	2	10	13
4) other.....	5	3	0	1	1
	67	19	5	18	25

for a few with slight mental deficiency and these are seen in the other groups, whereas the severely retarded belong to the bilaterally dilated symmetrical systems.

Table 29
Mental retardation in relation to type of P.E.G.

	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios	
	without displacement	with displacement		without displacement	with displacement
Mental retardation, all grades, combined with:					
1) motor handicap.....	20	1	0	6	3
2) epilepsy.....	12	2	1	0	1
3) motor handicap and epilepsy....	32	6	2	10	13
4) other.....	1	2	1	0	0
	65	11	4	16	17

Table 30

Relationship between degree of mental retardation and ventricular dilatation in 59 patients

	≤ 0.29	0.30-0.34	0.35-0.39	0.40-0.49	≥ 0.50
I.Q. > 55 + slight retardation.....	5	9	4	4	3
I.Q. ≤ 55 + severe retardation.....	2	9	6	10	7

The degree of mental retardation has been related to the ratio (Table 30). In a number of cases no I.Q. or developmental tests were performed and one had only a clinical impression of the intelligence, and this in the severe degrees of oligophrenia has been paralleled to the groups with I.Q.'s below 55. Whether it is justifiable to place the lesser degrees of retardation in the group debilitas (I.Q. 55-75) is not quite certain. Nevertheless, it seems useful and it is shown that a considerably higher number of high ratios occur in the severely retarded group. In the slightly retarded group we find that of 25 children, 11 have, ratios above 0.35, and in the group with the poorest intellect 23 of the 34 patients have ratios above this. With regard to prognosis, the symptoms do not add anything in particular to the suggestion already put forward that the more the system is dilated the worse is the prognosis. Children with a combination of motor symptoms, convulsions and oligophrenia had the poorest prognosis. Approximately 50% of the fatal cases showed this combination of symptoms. Not all the patients with these symptoms had a hopeless prognosis; 4 are to be found in the improved group at the time of follow-up as compared with the initial examination, e.g. a boy whose I.Q. was initially 54 increased to 80-90. He had the clinical picture of infantile spasms and E.E.G. revealed hypsarrhythmia. He is an example of a child who does well without steroid therapy.

The patients who did best were those whose symptoms fell outside the three major types (Table 31), and among these many were healthy at the time of follow-up. This can be explained by the lesser symptoms, e.g. headache, dizziness etc. which were the indications for P.E.G.

Of 180 patients with convulsions 56 had improved at the time of follow-up; these were mainly children with a slight degree of dilatation. Twenty-six of the motor handicapped children had improved, whereas only a few of the mentally retarded were improved.

In the present material it is not possible to attach any prognostic value to a particular symptom, but the different clinical pictures combined with certain degrees of ventricular dilatation are of importance. The symptoms at the time of recognition of the disease and at the time of admission are not

Table 31

Symptoms other than epilepsy, motor or mental handicap

	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios		Total
	without displace- ment	with displace- ment		without displace- ment	with displace- ment	
Headache (+ other possible conditions).....	11	0	0	0	1	12
Fractured skull + symptoms....	2	0	0	0	0	2
Tendency to fall, + possible dizziness.....	2	0	0	0	0	2
Restlessness, irritability etc.....	3	0	0	0	1	4
Large head circumference.....	2	0	0	1	0	3
Blindness, nystagmus.....	1	2	0	0	0	3
Pubertas præcox.....	0	1	0	0	0	1
Pains, blurred vision.....	0	0	1	0	0	1
	21	3	1	1	2	28

necessarily the same, e.g. a child may show signs of convulsions in the first twenty-four hours of life, and they may cease later, whereas the clinical picture may have changed to a tetraplegia and/or oligophrenia.

M: SYMPTOMS AND TIME OF RECOGNITION OF THE DISEASE IN RELATION TO THE P.E.G. FINDINGS AND FOLLOW-UP EXAMINATION

In the following we try to relate briefly the time of recognition of the disease, the P.E.G. findings and the prognosis. Sixty-six patients had symptoms manifesting themselves within the *first twenty-four hours of life*. This mainly concerns such symptoms as convulsions, rigidity, cyanosis, flaccidity and hypotonia. The prognosis is poor in all these groups, and particularly so in the first two. The best prognosis, although not very hopeful, was found in a group of hypotonic patients. The P.E.G. findings were mainly symmetrical dilatations and were frequently accompanied by a high ratio and a large third ventricle.

A number of patients with rigidity in whom the prognosis was poor had cortical air collections which could be better explained if one regarded the rigidity which occurred within the first twenty-four hours of life as an early symptom of a later developing tetraplegia or hemiplegia.

In 22 patients whose symptoms were recognised between the *second and fourteenth day of life* convulsions were a frequent and serious symptom. In addition, a few patients had severe cyanosis and one child had projectile vomiting and was thought to have pyloric stenosis. Another patient had a severe coli infection, poor general condition and severe dehydration. At

the time of follow-up this patient was normal. In this group the ventricular dilatations were mostly symmetrical, and the condition at the time of follow-up corresponds well to the degree of dilatation as shown by the ratio. Among those who died there were many with large third ventricles.

Twenty-one patients had symptoms which appeared between *two weeks and three months* of age. The findings were similar to the above-mentioned but the prognosis was perhaps better. In this group convulsions dominate the picture and the main P.E.G. finding was bilateral ventricular dilatation.

Sixteen patients showed symptoms between *three and six months* of age, and this group consists at the time of follow-up of 3 who had died, 5 under institutional care, 5 with handicaps and 3 healthy. Again convulsions were the main symptom though in some cases not always the first. One child had a bout of severe vomiting, and another prolonged crying spells before the convulsion appeared.

The 3 healthy patients all had convulsions as their first symptom which indicates that not only is it the most frequent symptom but is also connected to all degrees of prognosis. The 3 healthy patients all showed small degrees of dilatation.

Twenty-three children had their symptoms recognised between *six and nine months* of age, and of these 6 were dead, 6 under institutional care, 5 handicapped and 6 healthy at the time of follow-up. Convulsions were the most frequent symptom, and in one child these may have been febrile. One child in the handicapped group had had meningitis with severe P.E.G. changes including a third ventricle of 13 mm. It will probably never be known whether this finding was due to a transitory blockage of the cerebrospinal fluid circulation because the child has done well since and here has been no indication for further P.E.G. It is not possible to decide whether P.E.G. in such a case had the effect of loosening adhesions or of some similar action.

Only 10 patients showed symptoms between *nine and twelve months* of age. None of these have died. Four are under care and 4 show different handicaps. In this group one began to find that the P.E.G. changes were more often unilateral than in the previous groups. Convulsions were still a major symptom but in a number of these patients there was a long interval between the first and subsequent convulsions; in one child the interval was from the age of nine months to nine years.

Of 18 children with symptoms appearing from *one to two years* of age 3 have died. All 3 had had convulsions, 2 with long intervals between the first and subsequent convulsions. Both these patients were older, one fourteen and the other thirty-three at the time of death, and one cannot definitely relate the cause of death to the course of the disease.

The children with slight handicaps, or who were practically normal, had also had convulsions. Two of these were convulsions accompanying whooping-

cough and measles encephalitis. In one case the convulsions were psychogenic in origin.

In the following age groups the number in each year was small but the characteristic finding was convulsions which was the most common symptom in the whole material; this was followed by motor handicaps and mental retardation in a decreasing number. It was not surprising that the children had to be of a certain age before such disorders were sufficiently pronounced to justify investigation and P.E.G. Those who died in these age groups frequently had disorders which could be considered progressive. One child showed symptoms from the age of two years and died at the age of ten with symmetrical lesions of the basal ganglia, medulla and spinal cord (*Christensen, Melchior and Plum* 1956), the oldest lesions located cranially, the most recent caudally.

As can be seen from Table 25, an increasing number of unequal and displaced ventricular systems were found by P.E.G. and more and more small third ventricles. The prognosis for the age groups above 2 years of age was much better than before (Table 26).

As far as the 9 children are concerned, it was impossible to obtain explicit information on the exact time of recognition of the disease. It seems reasonable to assume however that the disease began in the first twelve months. Two of the children were examined at the age of eight months and others between one and two. One was examined at three and a half years and at that time it was said that he had always had convulsions and been retarded. This patient was drowned when he fell through a hole in the ice in the harbour a few years later. Finally, one patient was examined at the age of eight years and it was said that he had always been backward. Of the 9 children 4 had died, 4 were under institutional care and one had a motor handicap. Of the 4 who died one was rigid, one was premature and both died before the age of eighteen months. One child was admitted because of a weak back and it was said that he had always been retarded. The 4 children who were under care had all been retarded in development and had had convulsions. In conclusion, regarding the time of recognition of the disease, one can say that there is a definite dividing line at about the age of two years. Before two years 20% were healthy and the earliest age groups showed the fewest normal children. From two to fourteen years 60-70% were healthy and in the group aged eight to ten years 82% were healthy. If one looks at the small group with symptoms with an indefinite time of onset, this presumably belongs to the group of patients whose disease was recognised early, and corresponds to the follow-up result which revealed a poor condition. It would appear that if the disorder was not recognised until the age of two, the prognosis was considerably better than if the disorder was recognised before that.

Further indications of poor prognosis in the first years of life may be found in the presence of cortical air. Of 48 patients with an abnormal amount of cortical air, 41 showed symptoms before the age of one year. To these may

be added 2 more who belong to the group in which the time of onset of the disease was uncertain, but who were presumably ill before the age of one year. The remaining 5 patients with cortical changes were made up of a single patient in each of the groups 1, 2, 3, 6 and 7 years of age.

It had been emphasised in a number of previous reports that the changes of the sub-arachnoid space cannot be judged from the P.E.G., at least not before two years of age (*Grävinghoff, Zellweger*). A great number of the children in the present material were examined much earlier than this. That cortical air should be an accidental finding was unacceptable to the author. On the one hand the criteria for considering cortical air findings abnormal were rigid, and on the other these patients had a poorer prognosis than the patients in the present material which supports the evidence that the P.E.G. changes were real.

N: THE AETIOLOGICAL FACTORS RELATED TO P.E.G. FINDINGS AND FOLLOW-UP EXAMINATION

On p. 66 the various aetiological factors among the 271 patients were recorded. In the following the different forms of P.E.G. as seen in the different aetiological groups and their prognosis will be discussed.

A *familial predisposition* to nervous or psychiatric disorders was found in 52 patients, and these were the only aetiological factors in 6. Of these 6 patients one was dead, 3 were under institutional care and 2 handicapped to such an extent that they were unable to look after themselves at the time of follow-up examination. Among the 46 patients who, besides having a familial predisposition, had other aetiological factors, 9 cases were considered mainly familial and of these 9, 2 were dead, 2 under care, 3 handicapped and 2 healthy at the time of follow-up. When the P.E.G. findings in these 15 children were examined it was seen that the familial predisposition was of greater importance than the degree of ventricular dilatation. Most of them had ratios around 0.30 and there were no large ventricles. As previously seen, the patients who were in the worst condition had the largest ratios. Among 10 patients where familial predisposition was found to be as important as other factors, one was healthy, 5 handicapped, 3 under institutional care and one had died at the time of follow-up. In this group there were 3 patients where the existence of a similar complaint among siblings could explain an accompanying hearing disturbance and apart from this all 3 are healthy now. Dilatation was not marked in this group either but the variation was more pronounced than in the first group. In the remaining 24 patients where other factors were considered of greater importance than the familial predisposition, 6 were healthy, 4 handicapped, 9 under institutional care and 5 dead. In this group were found the most pronounced degrees of dilatation with ratios above 0.50. Some of these children had very large third ventricles (maximum 21 mm.).

Of the 52 patients with a possible familial predisposition 12 were healthy 14 had miscellaneous handicaps, 17 were under institutional care and 9 had died.

P.E.G. showed fairly small changes especially in the patients where the family predisposition was considered of major importance, and this can be interpreted that a familial predisposition in itself is of serious prognostic implication even if the ratio is of a moderate size, and the outcome will frequently be poor.

Prenatal aetiological factors were found in 50 cases and as the only possibility in 6. Of the 6, 4 had died, one was under institutional care and one was handicapped. As seen from Table 7, the group of mothers concerned had hypertension, severe vomiting and pyuria during pregnancy. In the case of the patient who was handicapped, the mother had had a severe shock in the sixth month of pregnancy. P.E.G. revealed severe dilatation, including third ventricles, and in one case there was porencephaly and severe cortical damage.

Birth trauma and asphyxiation were found, in 18 of the 44 patients who had prenatal factors in combination with other factors. Of these 18 children 2 were healthy, 4 handicapped, 8 under institutional care and 4 dead. P.E.G. showed some variation but mostly severe bilateral dilatation and dilatation of the third ventricle.

Of the remaining 26, 12 cases were healthy, 4 handicapped, 8 under care and 2 dead at the time of follow-up.

It can be seen from these figures that prenatal factors alone or combined with perinatal damage made the prognosis in this group very poor, whereas combined with other factors, where they are considered of major importance, the prognosis was considerably better. P.E.G. changes were generally severe except in cases where other possibilities were considered more important than the perinatal factors.

In discussing aetiological factors, *prematurity* was placed between prenatal and perinatal factors. In 11 children prematurity was the only aetiological factor, and in this group one was healthy, 4 had miscellaneous handicaps, 2 were under institutional care and 4 dead. Among 21 children who, besides prematurity, had other aetiological factors, 8 were healthy, 9 under institutional care and 4 dead. In 7 cases prematurity was combined with asphyxiation and these cases were not associated with a particularly poor prognosis.

In this small group there was no correlation between a low birth weight and a poor prognosis, or between a low birth weight and severe P.E.G. changes. The ratios varied from 0.30 to 0.50 but the third ventricles were rather large in this group, most of them measuring 5-7 mm. or more (maximum 16 mm). As mentioned, there were a number of patients who were said to have had a premature birth but this was not confirmed by the birth weight. It is impossible to exclude them all for some could have been premature, but in most of the cases

there were other and more acceptable aetiological factors to justify their inclusion in other groups. There was frequently the possibility of perinatal damage and in other patients information concerning familial predisposition was obtained at the time of follow-up.

Three patients with supposed prematurity as the sole aetiological factor, but whose birth weights were between 2700 and 3700 g. all had a bad prognosis. One was in a mental institution and 2 had died at the time of follow-up.

Perinatal factors as the only aetiological factor were found in 57 patients and in 78 were combined with other factors. Of the 57 patients 22 were asphyxiated for varying periods and 17 had prolonged deliveries. Of 12 patients with asphyxiation for more than 15 minutes 5 were healthy, one was handicapped, 4 were under institutional care and 2 dead. In only 3 patients asphyxiation was of short duration and all were under institutional care. In 7 patients it was not possible to obtain any information on the duration of asphyxiation; 2 of these had motor handicaps, one was under institutional care and 4 had died. Of the 17 children with difficult deliveries, 2 were normal at the time of follow-up, 6 had miscellaneous handicaps, 6 were under institutional care and 3 were dead.

The remaining 18 patients with perinatal aetiology fell into a number of different groups e.g. precipitate delivery, high birth weight etc. Of these one was healthy 5 were handicapped, 5 under institutional care and 7 died later. The P.E.G. changes in these children were mainly bilateral; the ratios varied in size and, as previously stated, the smallest ratios had the best prognosis. In the group with poor prognosis some had marked dilatations with ratios of 0.50 or more. A great number of the patients in this group showed large third ventricles, several above 10 mm. in width.

Perinatal factors were combined with other factors in 78 children. There was frequently a combination of postnatal factors and it was not possible to judge which was the most important in each case. In this group 28 were healthy, 14 handicapped, 22 under institutional care and 14 dead at the time of follow-up. A variety of P.E.G. changes were found but there were fewer unilateral dilatations and severe displacements than in the postnatal group. The third ventricles also varied and several were dilated to more than 10 mm.

Postnatal aetiology as the only factor was found in 58 patients, head injuries in 34 and head injuries and infection combined in 5. The prognosis for the 34 patients with head injuries was related to the age at the time of injury. Fourteen children were below the age of 3 at the time of injury; of these 3 were healthy, 5 handicapped in varying degrees, 2 were under institutional care and 4 were dead at the time of follow-up.

Of 20 children who sustained injury after the age of 3, 16 were well and 4 were handicapped. There had been no deaths and none of the children was under institutional care. This gives quite a different picture from that of the

children with early trauma. This may be explained by the much more mature development of the brain in the older age groups where the lesion is less likely to extend to areas other than those directly affected.

Of the 5 children who had trauma and infection and were worse at follow-up, 4 showed motor or mental handicaps and one had died.

Seven patients had post-infective conditions; of these, 3 were normal, 2 handicapped and 2 under institutional care. In 7 children the symptoms were preceded by febrile episodes and possibly febrile convulsions. Of these, 2 were healthy, 3 handicapped, one was under institutional care and one dead.

The last sub-group of postnatally acquired diseases consists of 3 patients who developed C.N.S. symptoms following whooping-cough, and here there could be a mechanical, traumatic or post-infective explanation, (cases no. 60, 130 and 160). Of these 3 the patient with the earliest symptoms was under institutional care and the other 2 were healthy at follow-up.

P.E.G. findings, especially in the group of post-traumatic conditions, showed only slight dilatations with ratios below 0.30 and frequently unilateral changes. The children with post-infective conditions showed severe changes and it was surprising that even though a number had large ratios, they did well. This might be explained by the fact that the P.E.G. findings were the result of transitory blockage due to oedema, hyperaemia, or to the fact that adhesions were loosened by the insufflation of air. In this group, too, it was found that a mature C.N.S. did better than an immature C.N.S.

Fifty-four children had other aetiological factors as well as postnatal factors. At the time of follow-up 24 were healthy, 11 handicapped, 9 under institutional care and 10 dead.

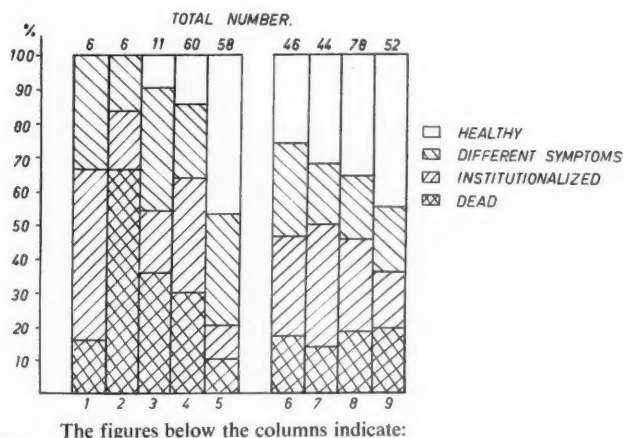
P.E.G. in these mixed groups varied much more than in the postnatally acquired group, but there were relatively large numbers of unequal ratios, unilateral dilatations and displaced systems. The relationship between the aetiological factors and the follow-up results can be seen in Fig. 35.

The importance of age at the time of onset of the disease can be seen from the follow-up of patients with no definite aetiological information. Their prognosis depends partly on the time of onset of the disease and partly on the degree of dilatation of the ventricular system. This applied to 24 patients, of whom 8 were healthy, 3 handicapped, 6 under institutional care and 7 dead.

In conclusion, patients on whom we have information concerning family predisposition have a poorer prognosis than one would expect from the degree of dilatation of the ventricular system. Patients with prenatal aetiological factors have the worst prognosis and frequently have large ventricular systems, including third ventricles. Perinatal factors lead to P.E.G. changes, mostly bilateral dilatation with variable ratios. Asphyxia of long duration was no worse as regards prognosis than asphyxia of short duration. The postnatal factors can be divided into post-traumatic and post-infective, and they have a better

Fig. 35.

AETIOLOGY COMPARED WITH THE FOLLOW-UP RESULTS



The figures below the columns indicate:

1. Familial predisposition.
2. Prenatal factors.
3. Prematurity.
4. Perinatal factors.
5. Postnatal factors.
6. Familial predisposition combined with other factors.
7. Prenatal factors combined with other factors.
8. Perinatal factors combined with other factors.
9. Postnatal factors combined with other factors.

prognosis than the other groups, especially traumatic conditions which showed a large number of unilateral and asymmetrical P.E.G. findings. Post-infective conditions included some cases with severe P.E.G. changes, large ratios and large third ventricles. At follow-up some of them had done better than expected.

O: X-RAY OF THE SKULL IN RELATION TO P.E.G. FINDINGS AND FOLLOW-UP RESULTS

As can be seen on p. 82. X-ray of the skull was performed in the Neuro-surgical Department on 186 of the 271 patients and the findings are recorded with the different types of P.E.G. in Table 32. The only remarkable finding was the high number of increased digital markings in the group with unilateral changes but the figures are too small to be significant. When compared with the results of the follow-up examination (Table 33) it was seen that a normal skull X-ray in the group with ratios between 0.30 and 0.39 was a good prognostic sign. The only group in which most children had a poor prognosis was the one showing changes in shape (scaphocephaly, brachycephaly etc.), and here the children were found to be unchanged or worse.

Table 32

Skull X-rays in relation to P.E.G. findings

Skull X-ray findings	P.E.G. findings:				
	Bilateral dilatation with same ratio on both sides		Unilateral dilatation	Bilateral dilatation with different ratios	
	without displacement	with displacement		without displacement	with displacement
Normal.....	44	16	5	16	14
Increased digital markings.....	17	1	6	1	2
Deep posterior fossa.....	15	4	0	3	2
Suture diastasis.....	6	0	0	1	0
Calcification.....	4	1	0	1	0
Changes in shape.....	11	2	2	3	1
Thin cranial bones.....	5	0	0	0	1
Bone defects (+ fractures).....	4	3	1	1	4
Pronounced venous grooves.....	8	0	0	0	1

Table 33

Skull X-rays in relation to follow-up results

	Improved	Im- proved- unchanged	Unchanged	Un- changed- worse	Worse	Dead
Normal.....	33	7	18	8	11	18
Increased digital markings.....	13	2	2	4	1	5
Deep posterior fossa.....	13	0	3	3	3	3
Suture diastasis.....	5	0	0	1	0	1
Calcification.....	2	3	0	0	0	2
Changes in shape.....	4	0	4	4	6	1
Thin cranial bones.....	3	0	2	1	0	0
Bone defects (+ fractures).....	4	4	1	2	2	0
Pronounced venous grooves.....	5	1	0	0	2	1

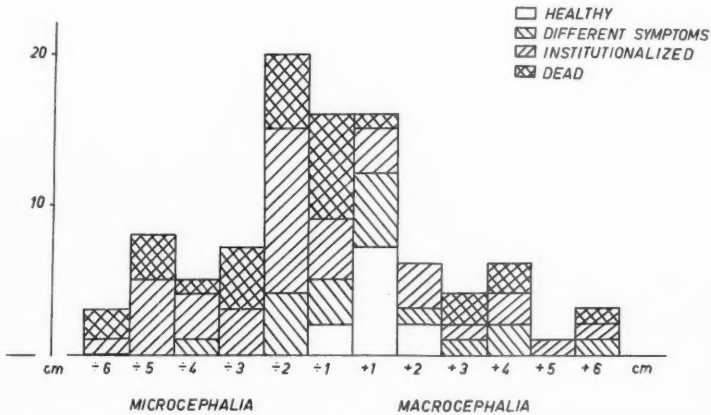
P: MICRO- AND MACROCEPHALY IN RELATION TO P.E.G. CHANGES
AND FOLLOW-UP RESULTS

With regard to changes in shape of the skull, both increase and decrease in circumference may be mentioned. Head circumference was measured in most cases, and these measurements were compared with the normal curve used in

the Paediatric Department (*Mitchell-Nelson*). Deviations of a centimetre below normal constituted a bad risk and the prognosis deteriorated with increasing deviation from the normal (Fig. 36). Similarly, ratios above 0.35 in cases of microcephaly were the most serious. Below this value some do relatively well.

Fig. 36.

DEVIATIONS OF HEAD CIRCUMFERENCE
COMPARED WITH THE FOLLOW UP RESULTS



Ordinate = no. of children. Abscissa = deviation of head circumference.

It does not seem necessary to have a correction of the ratio with regard to prognostic value in cases of microcephaly, as the ratio still expresses the distribution between brain tissue and the ventricular system. If the amount of tissue present is small it is understandable that a mild dilatation of the ventricular system may have serious consequences.

It is possible that in cases of macrocephaly there is some sort of compensatory factor which allows the remaining brain tissue to function better and this may explain the better prognosis.

From Tables 34 and 35 it may be seen that with a head circumference 2 cms. below normal, 5 patients were improved, 12 unchanged and 19 worse. With a head circumference more than 2 cms. below normal, 8 were unchanged and 15 worse. With the head circumference not more than 2 cms. above normal, 11 were improved, 7 were unchanged and 4 worse. With a difference of more than 2 cms. above normal 4 were improved, 3 unchanged and 7 worse at the time of follow-up.

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Ratio	Head circumference						
	+ 1 cm	+ 2 cm	+ 3 cm	+ 4 cm	+ 5 cm	+ ≥ 6 cm	total
≤ 0.29.....	1 i —	1 i 1 w	— —	— —	— —	— —	2 i 1 w
0.30–0.34.....	3 i 2 u —	1 i — —	— — —	— — 2 w	— — —	— — —	4 i 2 u 2 w
0.35–0.39.....	4 i 2 u 1 w	— 1 u —	1 i 1 u 1 w	— — —	— — —	— — —	5 i 4 u 2 w
0.40–0.49.....	— 2 u —	1 i — 1 w	— — —	2 i 1 u 1 w	— — 1 w	— — —	3 i 3 u 3 w
≥ 0.50.....	— — 1 w	— — 1 w	— — —	— — —	— — —	1 i 6 cm 1 u 10 cm 1 w 7 cm	1 i 1 u 3 w

Key

i = improved u = unchanged w = worse

Macrocephaly in relation to ratio and follow-up results

Ratio	Head circumference						
	+ 1 cm	+ 2 cm	+ 3 cm	+ 4 cm	+ 5 cm	+ ≥ 6 cm	total
≤ 0.29.....	1 i —	1 i 1 w	— —	— —	— —	— —	2 i 1 w
0.30–0.34.....	3 i 2 u —	1 i — —	— — —	— — 2 w	— — —	— — —	4 i 2 u 2 w
0.35–0.39.....	4 i 2 u 1 w	— 1 u —	1 i 1 u 1 w	— — —	— — —	— — —	5 i 4 u 2 w
0.40–0.49.....	— 2 u —	1 i — 1 w	— — —	2 i 1 u 1 w	— — 1 w	— — —	3 i 3 u 3 w
≥ 0.50.....	— — 1 w	— — 1 w	— — —	— — —	— — —	1 i 6 cm 1 u 10 cm 1 w 7 cm	1 i 1 u 3 w

Key

i = improved u = unchanged w = worse

Q: E.E.G. FINDINGS IN RELATION TO P.E.G. FINDINGS AND
FOLLOW-UP RESULTS

The last examination to be related to the other findings is the E.E.G. This was carried out on an increasing number of patients over the years and is now a routine examination. The E.E.G. reports used were those made by the E.E.G. department's medical staff.

As it is outside the scope of the present work to discuss these examinations in detail, only those gross changes which can be related to P.E.G. findings will be considered.

The relationship between E.E.G. and P.E.G. can be seen from Tables 36 and 37. As expected, there was a relationship between focal E.E.G. changes and asymmetrical and unilateral ventricular dilatations. Normal E.E.G.'s were found more frequently in symmetrical bilateral dilatations than in other forms and it can be seen that where the ratio was below 0.30 the E.E.G. was rarely

Table 36
E.E.G. findings in relation to P.E.G. findings

E.E.G.	Bilateral dilatation with the same ratio on both sides		Bilateral dilatation with different ratios		Unilateral dilatation	
	without displacement	with displacement	without displacement	with displacement	without displacement	with displacement
Normal.....	15 (9)	4	1 (1)	2	1 (1)	0
Possible changes.....	14 (5)	3	5 (1)	3	2	1
Diffuse changes.....	50 (7)	5	12 (3)	7 (1)	2	2
Focal changes.....	19 (3)	6 (2)	7 (1)	12 (3)	1	5
Diffuse and focal changes .	1	1 (1)	2	0	1	0
Total no. of E.E.G.s.....	99	19	27	24	6	3
No E.E.G.	53 (4)	12 (2)	7 (2)	16 (2)	0	0

The figures in brackets represent the number of cortical changes

Table 37
E.E.G. findings in relation to the degree of ventricular dilatation

	E.E.G. normal	Possible changes	Diffuse changes	Focal changes	Diffuse + focal changes
≤ 0.29.....	2	7	13	7	0
0.30-0.34.....	9	9	24	26	2
0.35-0.39.....	10	5	22	6	0
0.40-0.49.....	2	5	10	6	1
≥ 0.50.....	0	2	9	5	1
Total...	23	28	78	50	4

normal. This may be due to the high incidence of convulsions in the present material as convulsions combined with abnormal E.E.G.'s were frequently the indication for P.E.G.

E.E.G. changes were related to the age of the patient and it can be seen that *an abnormal E.E.G. in the age group below one year was a poor prognostic sign*. Of 41 children with this finding only one was doing well at the time of follow-up, 3 had miscellaneous handicaps, 19 were under institutional care and 18 were dead. A normal E.E.G. in this age group does not exclude a poor prognosis, e.g. of 8 children 3 had done well, 2 had minor intellectual defects and 3 were dead.

It might be expected that E.E.G. changes could be related to the finding of abnormal cortical air and the correlation between these factors and follow-up examination can be seen in Table 38. Not less than 11 of the 38 examined showed a normal E.E.G. and of the 27 with abnormal E.E.G.'s one was healthy, 6 had miscellaneous handicaps, 9 were under institutional care and 11 were dead.

Finally, the possibility of a special relationship between severely dilated third ventricles and E.E.G.'s was examined but none was found, e.g. no

Table 38
Relationship between E.E.G., cortical changes and follow-up results

E.E.G.	Cortical changes		
	generalised	unilateral	localised
Not done	2 dead 1 under care 2 slightly retarded	1 handicapped	2 dead 2 under care (idiot)
Normal	2 dead 1 handicapped	1 dead 1 under care 1 healthy	1 dead 2 under care 1 handicapped 1 healthy
Possible changes	1 dead 1 under care 1 handicapped	1 dead	2 under care
Diffuse changes	2 dead 2 under care 1 handicapped	1 dead	3 dead 1 under care 1 healthy
Diffuse and focal changes			1 handicapped
Focal changes	3 dead 3 under care 1 handicapped	1 handicapped	1 handicapped

particular E.E.G. finding was found to apply to patients who had third ventricles of 8 mm. or more. On the other hand, almost all these patients showed E.E.G. changes.

In conclusion, it can be said that X-ray examination of the skull did not throw any particular light on the prognosis in this material except that normal findings in the presence of moderate degrees of dilatation was a good sign.

A small head circumference had a worse prognosis than one would have expected from the ratio alone, but a large head circumference was not of such significance and could possibly be regarded as a compensatory reaction.

The E.E.G. showed a correlation between focal changes and asymmetrical ventricular dilatations. An abnormal E.E.G. in children below one year of age was a poor prognostic sign. There was no good correlation between cortical changes and E.E.G.'s.

CHAPTER V

Repeated P.E.G.'s

Only a few reports on the results of repeated P.E.G.'s could be found in the literature (*Rupilius* 1934; *King* 1938; *Evans* 1942; *Crothers, Lord and McGinnis* 1942; *Heidrich* 1955; *Krischek* 1959), altogether concerning 45 patients and they all showed a good correlation between the different examinations, in that only a few with progressive disorders had increased dilatations whereas the majority were unchanged.

In the present material of 271 patients 63 had had more than one P.E.G. and it would seem to be of importance in evaluating the P.E.G. to see if the original findings could be reproduced, especially the ratios. Unfortunately, as seen in Table 39, it was not possible in all cases to measure the ventricular system, and in a few cases it was not possible to obtain the original X-ray pictures and, therefore, one has had to rely on the reports of the changes. Some of the examinations were carried out within a short space of time and this illustrates immediate reproduction. In a great number of cases P.E.G.'s were performed after several years' interval, and in such cases the examinations have to be related to follow-up results because some of the children had progressive disorders and increased dilatation might be expected. On the other hand it was not likely that a child who had been sick and had later almost completely recovered would be re-examined by P.E.G. The suggestion that a severely dilated ventricular system reverts to normal at the same time as the symptoms disappear cannot be excluded but will, as stated above, probably never be proved. If the P.E.G. changes decreased as the clinical condition deteriorated or remained static, this would suggest an inaccuracy in the examination itself.

Table 39 shows that a great number of patients underwent more than two insufflations and 3 patients had P.E.G.'s both before and after admission to the Neurosurgical Department. The cases in which repeated examinations were carried out during the one admission were not included in the table unless other results were available. Thirteen patients were subjected to more than one P.E.G. during the same admission. Nine of these had had P.E.G.'s at other times but the remaining 4 (cases no. 97, 139, 180 and 209) showed a close correlation between the examinations. In one case the filling of the ventricular system was not satisfactory at the first examination (ratio 0.41)

Table 39
Repeated P.E.G.

KEY
V = V.E.G. S = S.E.G. L = L.E.G. l = left r = right

The findings in each column consist of right-sided ratio/left-sided ratio, the third ventricle in millimetres, possible displacement of the ventricular system, the side to which it is displaced and the degree of displacement in millimetres. In the follow-up column R. and L. indicate right and left side. Filadelfia is a hospital for epileptics.

Case no.	Earlier findings	Interval	Findings on admission	Interval	Later findings	Follow-up
2	—	—	V: 29/25 3 mm	2 yrs.	29/26 r: - 7 mm	Healthy, married with 2 children
3	L: poor filling 0.30	1 mth.	V: 25/29 3 mm	—	—	Healthy, athlete etc.
14	L: 28/25	2 yrs, 1 mth.	S: 27/28 2 mm	—	—	Healthy, occasional epileptic symptoms.
25	—	—	V: 29/33 7 mm	4 yrs.	L: normal/little large	Home for epileptics, later married several times.
32	—	—	S: 32/30 5 mm	1 yr.	V: 33/32 6 mm	Slight headache, otherwise healthy.
37	L: 27/30 3 mm	1 mth.	V: 30/32 4 mm	—	—	In State institution, athetoid movements, microcephaly, hypsarrhythmia.
40	—	—	S: 29/34 4 mm	11 yrs.	L: 32/36 5 mm	Housework, epilepsy, psychogenic changes.
45	—	—	V: 32/32 8 mm	1 yr.	V: 35/35 1 mm L: 31/31	Died shortly after.
46	L: 31/31 4 mm	2 mths.	S: 32/32 5 mm	—	—	Healthy, rather brisk reflexes.
53	—	—	S: unsuccessful V: 31/35 5 mm	5 yrs.	L: 33/39 6 mm	Died in Filadelfia following accident, (rupture of liver). I.Q. 91-70
54	—	—	S: 35/31 7 mm	3 yrs. 6 yrs.	L: 32/32 L: 33/34 6 mm	Filadelfia. I.Q. 66 Slight neurological changes. Rare seizures.
63	—	—	V: 33/34 8 mm	9 yrs.	42/35 9 mm r: - 7 mm	Housework. I.Q. 1957: 55.

Table 39 (continued)
Repeated P.E.G.

Case no.	Earlier findings	Interval	Findings on admission	Interval	Later findings	Follow-up
64	—	—	V: cyst of septum pellucidum 34/33	1 yr. 5 yrs. 8 yrs.	S: 35/34 L: 38/32 L: 36/38 V: /32	Filadelfia. Occasional seizures. I.Q. almost normal.
68	—	—	V: 34/34 3 mm	1 mth.	L: 36/38	Died at 5 mths.
83	—	—	V: 32/35 8 mm	2 mths. 2 yrs.	L: 29/42 L: 28/36 r: - 5 mm	Rigidity and convulsions. Seizures, otherwise healthy.
84	—	—	V: 34/34	6 mths.	S: 35/33 10 mm	Slight motor retardation.
86	—	—	S: 33/34 10 mm V: 35/35 5 mm	7 yrs. 10 yrs.	L: 38/42 7 mm L: 38/49 11 mm	Home for epileptics. Debilitas mentis.
89	L: 31/34 9 mm L: 31/33 —	1 yr. 1 mth.	V: 36/34 9 mm	—	—	Died 1 mth. later, tetraplegia.
93	—	—	L: 34/35 6 mm	1 yr.	33/36 6 mm	Died 3 yrs., tetraplegia, seizures, oligophrenia.
94	L: 35/35 9 mm	2 mths.	V: 34/35 8 mm	—	—	Died. In State institution, apparently progressive for approx. 18 months.
95	—	—	V: 36/37 5 mm	5 yrs. 8 yrs. 10 yrs. 13 yrs.	L: 37/38 L: 33/38 L: 35/38 L: 36/40	Severe epilepsy, progressive physical deterioration with motor disturbance.
96	—	—	V: 36/35 3 mm	3 yrs. 6 yrs.	L: 36/38 L: 36/38	Died in treatment home.
99	—	—	S: 34/38 5 mm	2 yrs.	L: /39	Presumably healthy, bad tempered.
100	—	—	S: 35/37	2 yrs.	L: 40/44 5 mm r: - 5 mm	Earlier epilepsy. Now healthy.

Table 39 (continued)
Repeated P.E.G.

Case no.	Earlier findings	Interval	Findings on admission	Interval	Later findings	Follow-up
104	Some dilatation?	1 mth.	S: 37/36 15 mm	—	—	Large head, inferior intelligence, no seizures.
107	—	—	V: 37 13 yrs.	13 yrs.	L: slight dilatation of lateral vents. No displacement. L: 40/37 + 5th vent. 14 mm	Occasional seizures, R. hemiplegia, married and working. Died in Philadelphia when 18 years old. I.Q. 81.
110	L: 39/37. + 5th vent.	2 mths.	V: 38/36 (inc. 5th vent. 12 mm) (corrected to 30/30) V: 40/35 7 mm	2 yrs.	—	Oligophrenia, tetraplegia, microcephaly.
113	L: 41/36 8 mm	1 mth.	V: 36/40 4 mm	19 yrs.	L: dilated ant. horn	Cleaning work, rare seizures, right-sided deafness. Died 1 mth. later.
115	—	—	V: 38/39 V: septum cyst 41/41	2 mths. 6 yrs.	V: 37/42 4 mm L: diffuse dilatation	State institution. Tetraplegia, epilepsy, oligophrenia (idiot), inferior intellect.
120	—	—	V: 42/39 5 mm	4 mths.	S: 41/40	Oligophrenia (idiot), microcephaly.
134	—	—	V: 44/43 6 mm	1 yr.	S: 39/37 7 mm	Tetraplegia, aphasia, dysphasia, large head circumference, I.Q. almost normal.
138	L: 43/44 10 mm	1 mth.	V: 42/47 7 mm	—	—	Very poor general condition, oligophrenia, epilepsy, apparently progressive.
140	L: 42/42 12 mm	3 yrs.	V: 45/49 13 mm	—	—	Died.
153	—	—	V: 29/31 3 mm l: — 10 mm	8 yrs.	S: 28/34 5 mm l: — 15 mm	Epilepsy, I.Q. normal.
160	L: 29/33 5 mm l: — 10 mm	1 mth.	S: 30/34 6 mm l: — 11 mm	4 yrs.	S: 30/38 7 mm l: — 6 mm	

Table 39 (continued)
Repeated P.E.G.

Case no.	Earlier findings	Interval	Findings on admission	Interval	Later findings	Follow-up
170	—	—	S: 36/33 I: - 13 mm	3 mths.	V: 36/38 I: - 17 mm	Died one mth. later.
174	—	—	V: 37/34 I: - 6 mm	10 yrs.	L: 37/32 I: - 4 mm	Housework, mentally dull.
175	—	—	S: 37/37 I: - 10 mm	3 yrs.	S: 60/37 r. - 16 mm V: 74/37 3rd vent. 16 mm I: - 8 mm	Died. Tub. meningitis.
176	L: 32/34 I: - 8 mm	1 mth.	V: 39/35 I: - 11 mm	—	—	State institution, idiot, blind.
178	—	—	V: 43/41 I: - 11 mm	8 yrs.	L: 45/47	State institution, idiot, tetraplegia, epilepsy.
188	—	—	V: 19/25 I: - 11 mm	1 yr.	S: 23/29 I: - 11 mm	R. hemiplegia, I.Q. normal.
192	L: 27/34 I: - 18 mm	1 yr.	Following operation on r. side V: 20/34 I: - 10 mm	2 mths.	S: 32/34 I: - 19 mm	Healthy, working.
202	—	—	S: 27/36 I: - 10 mm	4 mths.	V: 29/37	Epilepsy (occasional seizures). I.Q. almost normal.
204	V: small and compressed (cannot be found).	7 yrs.	S: 36/27 I: - 10 mm	—	—	Slight R. hemiplegia. I.Q. 85. Occasional seizures.
212	L: normal system	1 mth.	S: 32/38 I: - 10 mm	4 yrs.	S: 34/44 I: - 11 mm	Training to be a plumber.
213	—	—	V: 33/39 I: - 10 mm	7 yrs.	V: 44/68 I: - 11 mm	R. hemiplegia, I.Q. slightly reduced.
227	L: 43/51 (48)	1 yr.	S: 38/58(47) 5 mm	14 yrs.	L: 1. > r. approx. 50	State institution, microcephaly, epilepsy, tetraplegia.

Table 39 (continued)
Repeated P.E.G.

Case no.	Earlier findings	Interval	Findings on admission	Interval	Later findings	Follow-up
232	—	—	V: 25/31 5 mm	1 yr. 4 yrs.	S: 25/34 5 mm l: - 9 mm L: 30/31 5 mm L: 28/33 4 mm l: - 16 mm L: unchanged	I.Q. ? Speech and hearing defect ? sight ? occasional seizures. Home for epileptics. Psychiatric difficulties.
233	—	—	V: 28/34 3 mm l: - 18 mm	8 yrs.		Oligophrenia (imbecile), occasional seizures. Filadelfia, I.Q. 59. R. hemiplegia.
235	L: 38/32 6 mm	3 yrs.	S: 36/27 5 mm r: - 6 mm S: 26/41 10 mm l: - 12 mm S: 27/35 8 mm + operation on left side	—	V: 20/41 8 mm L: 30/37 11 mm l: - 21 mm	Oligophrenia (inf. intellect), R. hemiplegia, congenital heart disease.
240	—	—	S: 40/27 6 mm r: - 8 mm S: 25/43 6 mm l: - 16 mm	1 yr. 5 yrs.	S: 42/27 r: - 10 mm S: 20/42 8 mm l: - 26 mm	L. hemiplegia, dysarthria, I.Q. almost normal. R. hemiplegia, epilepsy, psychiatric difficulties. I.Q. somewhat reduced.
241	L: r > l. (No useable pictures)	1 mth.				R. hemiplegia, epilepsy, I.Q. normal.
250	—	—	V: 34/41 10 mm r: - 6 mm	1 yr.	33/57 11 mm (Not good pictures) 28/84 11 mm l: - 12 mm L: 32/48 6 mm l: - 9 mm L: 31/40 3 mm l: - 11 mm	R. hemiplegia, epilepsy, I.Q. normal.
253	L: cannot be measured	4 yrs.	S: unsuccessful	1 yr. 3 yrs.		Psychopathy, epilepsy, inf. intellect ?
261	L: 37/44	1 mth.	V: 40/47 7 mm r: - 6 mm	—		R. hemiplegia (flaccid).

and at the second examination the ratio was found to be 0.46. The other 3 showed little or no variation.

That the examination result could be duplicated in cases where it had been carried out within a very short space of time supports the consistency of the procedure and this is also the case even if it has not been performed in the same department.

Six patients had had P.E.G.'s more than one year before admission. Of these, 3 were unchanged with regard to ratio. One patient showed a slight increase. This patient's clinical condition showed a tendency to progress and the condition at the time of follow-up was characterised by oligophrenia. Another patient had had P.E.G.'s performed previously showing small compressed ventricles following an acute injury. At the later examination a ratio difference was found, hemiplegia and occasional atypical convulsions. The last patient with a changed ratio was operated on between the two examinations and the ratio was smaller on the operated side at the second examination but later reverted to the previous size.

Thirteen patients had had P.E.G.'s less than one year before admission, and often immediately before. Eleven of these had unchanged ratios. One could not be assessed and one showed an increase on one side of 0.07. This patient was under institutional care and was almost blind.

Six patients were examined less than one year after admission, and of these 3 had the same P.E.G. finding. One had the same ratio but changed cortical air (case no. 170). This patient died. One patient, as mentioned above, was operated on, and one examination was shortly after this when the cerebrospinal fluid was leaking and papilloedema was present. When these symptoms disappeared the ratio became the same as before operation. The last patient in the group with changed ratios and an increasing unilateral dilatation had a rapidly progressive disorder and death ensued in a few months.

Thirty-seven patients were studied again more than a year later and in a number of cases several times. In some cases 10 years or more had elapsed since the original examination. In 5 patients only the reports of the examination were available so that the findings cannot be assessed with certainty. Of the remaining 32, 23 had unchanged findings at subsequent examinations.

The 9 patients with changed ratios include a patient who was first examined when a few weeks old, and then again a year later. In this case there was a change towards smaller ratios but the difference was only in the order of 0.05/0.06. This patient was mentally retarded and microcephalic, and was in a State institution. In another patient the ratio was a little less on one side at a later examination (0.06) but the findings were unchanged on the other. This patient was in a home for epileptics and had a chronic disorder.

In 3 cases there were small increases in the ratios, in one patient on one side alone. This patient was in an institution for epileptics. One patient had an increase of 0.05 to 0.07 and was doing well at the time of follow-up. Finally,

a child with changes of 0.02 and 0.06 was mentally retarded and under institutional care.

In 4 children there was a great increase in ratio. One had at a later examination a tuberculous meningitis which was fatal. Another patient had a constant increase on the left side. Her symptoms were convulsions and some psychiatric difficulties and an operation was being considered. One patient (case no. 213, figs. 37, 38 and 39) also suffered from convulsions and had an increased ratio on one side. This patient was operated on because of an atrophic lesion and her post-operative condition was much more satisfactory. The last patient showed a similar picture and hemispherectomy was performed recently, but in this case the period of observation was too short to comment on the changes in his condition.

Repeated P.E.G.'s have shown that the same findings can be easily reproduced. Only in a few cases is there a great difference and almost all these have disorders which can account for it. In the majority the findings were unchanged even after an interval of several years between examinations.

This is of great value with regard to the reliability of examinations and the usefulness of the ratio. Furthermore, it indicates that such a measurement can be performed even if one does not use absolutely standardised methods of insufflation and X-ray technique. On the other hand it must be mentioned that the Danish departments which carried out the P.E.G.'s presumably used the same techniques as the Neurosurgical Department but there could be small differences which nevertheless do not seem to have influenced the measurements to any great extent.

CHAPTER VI

Operations

Operations were performed on a number of patients. Some of these confirmed the P.E.G. findings; others revealed changes which were not obvious on X-ray, e.g. non-communicating cysts.

It is outside the scope of this present study to give details of operative procedures but it is of interest to make a brief summary of the possibilities involved. The operations together with data on the patients, sex, age and follow-up results are listed in Table 40.

It can be seen that in the cases where a meningo-cerebral scar or an area of atrophic tissue was removed the results were often good and at follow-up the patients had improved. In cases where the operation was for opening or removal of cysts, the prognosis was worse because cysts were often accompanied by severe changes in the brain, e.g. porencephaly after severe birth anoxia or prenatal malformations. Because the material is selected there are no operations for tumours, nor are there operations for reducing raised intracranial pressure.

Four patients with subdural haematomas had membranes removed, and one of these was peculiar because there was no history of trauma at birth or later, though a febrile disorder at the age of 7 months was diagnosed as encephalitis. At operation shortly afterwards inner and outer membranes were found and were thought to be a sequelae of haemorrhage as there were no signs of infection. At autopsy some years later it was still impossible to find any evidence of an infective aetiology.

Table 40
Survey of patients undergoing surgery

Operation	Case no.	Sex and age in years at operation	Specific position and findings	Follow-up
Removal of meningo-cerebral scar	2	f. 11		Healthy
	81	f. 9		L. hemipl., healthy
	173	m. 12		L. hemipl., epil.
	247	m. 11		Healthy
	253	m. 7		Epil., psychopath.
Removal of atrophic tissue and possible focus	5	m. 13	Osteitis	Healthy
	75	m. 3	Coagulation of temporal lobe area	Healthy
	153	f. 14	L. fibrous condition	Dead
	188	f. 6	L. abnormal vessels	R. hemipl., healthy
	191	m. 3	L. depressed fracture	Deaf, healthy
	192	m. 9	R. hemisphere lesion	Healthy
	213	f. 13	L. motor zone focus	R. hemipl., epil., intellectual inferiority
	233	m. 8	L. coagulation of vessels	R. hemipl., epil., intellectual inferiority
	258	m. 6	R. atrophic lesion	L. hemiplegia
Removal or opening of cysts	68	m. 2 mths.	R. Sylvian fissure	Died 3 mths. later
	72	m. 2	L. temporal lobe	Idiot
	84	m. 5 mths.	L. pia cyst, absence of septum pellucidum	Imbecile, tetrapl.
	147	m. 3	R. arach. cysts., perforation of septum pellucidum	Debilitas, tetrapl.
	159	f. 1	L. temp. lobe porencephaly	Idiot
	239	m. 9 mths.	L. intracranial cyst	R. hemipl., debil.
	261	m. 6	L. hemispherectomy, arachnoid cyst	
	269	m. 8	R. cyst	R. hemipl., I.Q. normal
Removal of haematoma membranes	8	m. 5 mths.	+ calcification	Died 2 years later
	112	f. 17 mths.		Died 4 years later
	184	f. 13	+ cyst	Healthy
	245	m. 16 mths.	+ scar	R. hemipl., epil., I.Q. slightly reduced

CHAPTER VII

Pathological findings

The pathological material was divided into three different groups according to the way it was obtained:

- A: Biopsy (20 cases).
- B: Examination of tissue removed at operation (15 cases).
- C: Autopsy findings (22 cases).

Most of the examinations were performed by Dr. Erna Christensen in the Rigshospital's Neuropathological Laboratory and the author was able to examine all the material and the reports. Some of the examinations were performed elsewhere and the author was able to examine most of the material.

Some of the case reports and pathological findings which will be discussed have been published already and reference may be made to them for more detailed information. Only the main points are included here for discussion.

The value of pathological examinations in relation to P.E.G. has been mentioned several times and a number of reports may be found in the literature (*Dannenbaum 1926; Guttmann 1929, Rupilius 1934; Kruse and Schaetz 1935; Bannwarth 1939, Malamud and Garoutte 1954*).

Autopsy provides the best opportunity of making a direct comparison between the X-ray findings and the disease process, even if removal of the brain, transport etc. has had some effect on the ventricular system. In the present study it has not been possible to standardise removal of the brain as in the anatomical studies of the ventricular system's size by *Knudsen (1958)* because the material has been collected from a number of different hospitals but, nevertheless, it gives a good idea of the degree of dilatation of the ventricular system.

A: BIOPSY FINDINGS

Biopsy findings can frequently give a good indication of the aetiology and the conditions of the cortex. At the same time the P.E.G. findings particularly concerning cortical atrophy are either confirmed or refuted.

Cortical biopsies obtained by needle puncture were performed on 20 patients and only small sections of tissue were removed, a fact that must be borne in mind when microscopic examinations are considered. The biopsy reports are as follows: normal cortical tissue, degenerative changes, dysplastic changes etc.

Microscopy revealed normal cortical tissue in 6 cases, slight chronic changes of ganglion cells with proliferation of glial tissue in 3 cases, destruction of ganglion cells in 3 cases, possible dysplasia of ganglion cells in one case, slight changes in ganglion cells and changes in the meninges in 2 cases, suspected lipoidosis or related disorder in one case, proliferation of inner layer of capillaries in one case and post-infective changes in 3 cases.

As can be seen from this survey it is the condition of the ganglion cells which has frequently raised the suspicion of pathological conditions. As the examination is mainly concerned with the condition of the cortex, it is of interest to compare it with the abnormal cortical air collections. Of the 6 normal cortical findings 4 were in children who did not develop normally. Of these 4 children, one aged six months had an excess of air on the cerebral surface, especially frontally, and the other 3 did not reveal any abnormal cortical air findings. Of the 2 who were healthy at the time of follow-up one had a moderate amount of surface air and the other was normal. Of the 14 who had pathological findings at microscopic examination 5 had abnormal cortical air collections. The pathological findings were ganglion cell degeneration, proliferation of glial tissue and meningeal changes.

If the biopsy results are related to the clinical condition and the follow-up results, the following sub-groups can be established:

- (a) Biopsy report supporting the diagnosis and corresponding to the follow-up result. (7 patients, cases no. 94, 125, 137, 150, 151, 167, 216).
- (b) The biopsy, although suspicious, may be inadequate to support the diagnosis. This may be due to the small amount of tissue and to the fact that the biopsy is often taken at the time the V. E. G. is performed. The same burr hole is used and this may not be directly over the area under suspicion, (cases no. 84, 105, 113, 129, 176, 222, 231, 235, 268).
- (c) A normal biopsy which is not in keeping with the clinical course (4 patients). This may be due to the reasons given in (b), (cases no. 37, 209, 256, 259).

There may be a fourth group where the biopsy report suggests a major disorder which is not however confirmed at follow-up. This may be a serious mistake because of the possible wrong prognostic implications and the institution of incorrect therapy. Such a group is not present in this material.

In conclusion it may be said that, even considering the small biopsy sections available, a positive result or at least suspicion of changes was obtained in 16 of 20 examined, and only in 4 cases the results did not correspond with the clinical findings. In no case did the biopsy findings lead to an over-pessimistic prognosis.

B: EXAMINATION OF TISSUE REMOVED AT OPERATION

Altogether 15 specimens were still available for histological examination. One is excluded from this report as it was a bone section.

The tissues examined fall into the following main groups:

- (a) Meningo-cerebral scars, (5 patients, cases no. 2, 81, 173, 247, 253). Of these 3 were healthy at the time of follow-up and 2 had handicaps which were mainly psychological. Among the healthy patients one had a hemiplegia which did not trouble him. Two of the patients had early cyst formation besides scar formation, and both had had brain abscesses removed.
- (b) Glial scars were found in one case (case no. 72). This patient had a difficult birth and at three weeks of age otitis media and meningitis. The patient is now under institutional care and is an idiot and microcephalic.
- (c) Atrophic lesions, (2 patients, cases no. 213, 258). One had had a birth injury and the other an injury when he was six years old. Both had slight mental retardation and hemiplegia.
- (d) Arachnoid cysts. Three patients were operated on for arachnoid cysts, (cases no. 147, 239, 269). In 2 the P.E.G. showed the ventricular system to be unequally dilated and displaced away from the most affected side. At follow-up one of the 3 patients had a slight hemiplegia, one was under non-institutional care and one had a slight tetraplegia. The patient with the tetraplegia was operated on recently and it is too early to comment on the outcome.
- (e) Sub-dural hygromas were removed from 3 patients, (cases no. 8, 112, 184). There was no history of trauma in 2. One had "encephalitis" at 7 months, as mentioned above, and the other pregnancy was complicated by increased blood pressure. There was insufficient information on the third patient as he was a foreigner. Two patients died and the third was well at the time of follow-up.

C: AUTOPSY FINDINGS

(a): *Mortality*

Before going into details of the autopsy results, the death rate for the whole material should be considered. Of the 271 children examined, 58 had died at the time of follow-up. Of the fatal cases 37 were boys and 21 girls which corresponds to the sex distribution within the whole material. Most of the children died before they were two years old and only 10 deaths occurred after the age of six and these include accidents and accidental poisoning (Table 41).

Table 41
Age at death

Age	Total deaths
0-11 mths.....	10
1- 1 yr. 11 mths.....	13
2- 2 yrs. 11 -	9
3- 3 - 11 -	6
4- 4 - 11 -	4
5- 5 - 11 -	6
6- 9 - 11 -	3
10-19 - 11 -	6
20 →	1

The most common cause of death in the younger patients was some kind of febrile disorder. The direct cause of death, as far as it is known, is shown in Table 42. It may be seen that not less than 42 of the 58 fatal cases had febrile disorders, 17 with pneumonia or bronchitis and 2 with infectious diseases (measles and chicken-pox). In one patient autopsy revealed tracheo-bronchitis and bronchiolitis but there was no history of previous febrile disorders in this case.

Table 42
Direct cause of death in the
58 patients

Fever of definite or possible cerebral origin:		
post-S.E.G. state.....	23	1
doubtful encephalitis.....		1
meningitis.....		2
Fever caused by possible or definite pneumonia and/or bronchitis....	17	
Tracheobronchitis (temp. not recorded).....	1	
"Childhood diseases".....	2	
Purulent meningitis without fever...	1	
Post-S.E. i. state without fever....	1	
Post-operative state.....	1	
Convulsion (? temp.).....	1	
Violent death.....	4	
accident.....		2
poisoning.....		2
Emaciation.....	4	
No information or indefinite information.....	3	
Total...	58	

Twenty-three had fever of cerebral origin. Some of these were suspected initially to be due to respiratory disorders but these were excluded at autopsy. In two cases meningitis was the cause of the fever and in a further case it was suspected. Another patient was thought to have encephalitis and this was confirmed at autopsy. S.E.G. was thought to have precipitated the temperature in one case. Undetermined encephalitis as the origin of cerebral fever, as suggested by *Casamajor*, is unlikely, and in many cases can be definitely excluded.

Of the 23 patients, 8 boys and a girl died less than 2 weeks after moving into new surroundings. This could be explained in some cases by exposure to infectious diseases. In others the febrile reaction may be neurovegetative in origin as seen after P.E.G. The mechanism of this febrile reaction could be due to a feeling of uncertainty or fear of the new surroundings, leading to the clinical picture described by *Cannon* (1942) as "Voodoo death", a picture which in recent years has been verified in animal experiments by *Richter* (1957). *Cannon* says: "Voodoo death may be real and it may be explained as due to shocking emotional stress – to obvious or repressed terror." For this reason one must consider antibiotic therapy as prophylaxis against the infection which may occur and at the same time treatment should be aimed towards reducing the temperature and calming the patient especially in the initial stages until the brain-damaged child has become accustomed to the new surroundings. This treatment can be established mechanically by cold baths etc. or by treatment with antipyretics, and finally a drug acting on the sympathetic nervous system may be of value.

(b) Autopsy results.

Autopsy results give a comparison between the changes seen on P.E.G. and the anatomical conditions in the brain. However, this is not always reliable because changes can occur after death. In the following the autopsies will be reviewed with regard to comparison between P.E.G. examination and the pathological findings. It is beyond the scope of the present work to review the vast literature on neuro-pathological changes in brain-damaged children in general or in special sub-groups but mention may be made of a few of the many textbooks on this subject, *Bumke and Foerster* 1936, *Russell* 1949, *Hicks and Warren* 1950, *Benda* 1952, *Courville* 1953, *Malamud* 1957, *Lubarsch, Henke and Rössle* 1957, *Greenfield* 1958, all of which contain a rich number of references.

In 9 cases autopsy was performed at other hospitals and when this has been the case the author has examined the material whenever possible or has had access to the original reports. Thirteen brains were examined in detail at the Psychiatric Laboratory. Three of the autopsy reports have been published: case no. 96 (*Christensen, Melchior and Plum* 1956), case no. 170 (*Brandt,*

Christensen and Vesterdal 1952) and case no. 217 (*Trojaborg and Plum 1960*), (*Christensen and Melchior 1960*). Details of the autopsies performed are given together with the aetiological data and the P.E.G. findings. Further clinical details can be obtained from the case reports.

Case. no. 53

Clinical summary: boy, two years of age, who had a head injury followed by loss of consciousness and left-sided convulsions. A depressed fracture was present in the right parietal region. V.E.G. performed at 8 years of age revealed a ratio of 0.31/0.35, third ventricle 5 mm. L.E.G. at 13 years of age revealed a ratio of 0.33/0.39, third ventricle 6 mm. The patient lived in a hospital for epileptics and died at the age of 13 after falling from a high tree.

Autopsy: a 16 cm. rupture of the liver was found. The cranium did not show new damage but the scar of an old fracture was present on the left side. The bone was thin over an area of 15 mm. and a small defect of 2-3 mm. was found in the centre. Corresponding to this area a fine adhesion was seen on the surface of the brain but no true scar formation.

Conclusion: unfortunately there was no microscopic examination or description of the ventricular system. There is disagreement concerning the site of injury because the fracture was originally found on the right side and at autopsy changes were found on the left side (? burr holes).

Case no. 103

Clinical summary: boy who was jaundiced from the first day of life until the age of one month, and at the same time had a severe degree of anaemia for which he received several blood transfusions. In the second month he was intermittently stiff and flaccid. On admission at eight months of age S.E.G. showed a ratio of 0.36/0.36, third ventricle 15 mm. There was an increased amount of cortical air especially on the right side. He became ill during the examination but recovered. Later he had repeated episodes of fever and was admitted several times to a paediatric ward. On his last admission at 18 months he was already dead.

Autopsy: mucus and stomach contents found in the trachea. One-third of the lung was collapsed. The brain showed moderate hyperaemia of the meninges. There was no obvious atrophy of the cortex or dilatation of the ventricular system and no signs of kernicterus. Microscopy showed hyperaemia and infiltration of monocytes and lymphocytes in the leptomeninges. Some of the large nerve cells showed degenerative changes and in a central area vascularisation appeared to be increased. There was clear differentiation between the cortical layers.

Conclusion: the changes found in the cortex corresponded to sequelae of iso-immunization, anaemia and consequent anoxic changes. The ventricular dilatation ratio of 0.36 was moderate. If the expression "no remarkable dilatation" can be interpreted as indicating some dilatation this fits in with the ventricular ratio.

Case no. 122

Clinical summary: boy with a family history of convulsions and mental retardation. Birth weight 4450 g. Rigid since birth. At two months of age had gastro-enteritis and seizures. On admission at 7 months S.E.G. showed a ratio of 0.39/0.39 and third ventricle of 2 mm. Large amounts of cortical air were found, especially on the right side and frontally as well as in the Sylvian fissure. His condition deteriorated and he was admitted to a paediatric ward. At 13 months his seizures increased and he died in hyperpyrexia.

Autopsy: this showed severe oedema of the leptomeninges. Autopsy diagnosis: sub-chronic right-sided sub-dural haematoma in the anterior cranial fossa. Sub-chronic epidural haematoma. Subcutaneous haematoma in the temporal region. Internal hydrocephalus following meningeal adhesions. Partial collapse and bronchopneumonia of the right lower lobe of the lung. Purulent bronchitis on right side.

Conclusion: it is impossible to decide which is the most likely aetiological factor. Malformation cannot be excluded but a more likely factor is the difficult birth. Birth injury could be responsible for the haematomas but these could also be due to extravasation of fluid as a result of the disorder which he had at two months of age. The site corresponds to the cortical air anomalies. Unfortunately the description does not allow evaluation of the presence of fluid, membranes etc. The diagnosis of internal hydrocephalus points to a dilatation of the ventricular system.

Case no. 148

Clinical summary: boy born four weeks prematurely. Birth weight 2650 g. Delivery was prolonged and was induced medically. The cord was round the neck and the patient was asphyxiated. When three days old he developed convulsions, neck stiffness, rigidity and nystagmus. Lumbar puncture showed bloodstained fluid. On admission to the Neurosurgical Department at 14 days of age V.E.G. showed a ratio of 0.69/0.67, third ventricle 4 mm. He died in hospital at the age of 2 months.

Autopsy: showed no abnormality except for a yellow membrane which was found below the right hemisphere of the brain and above the pons and peduncle. The cortex was 2-4 mm. thick. The cavities were filled with yellow serous fluid. There was no rupture of the falx or tentorium. Autopsy diagnosis: sequelae of sub-arachnoid haemorrhages. Occlusion of the foraminae of Magendie and Luschae. Internal hydrocephalus with atrophy of the cortex.

Conclusion: clinical findings, X-ray and autopsy all support the diagnosis of birth injury with haemorrhage and disturbance of the circulation of cerebrospinal fluid.

Case no. 149

Clinical summary: boy whose mother had abdominal pain during the entire pregnancy. Delivery was induced medically and was four weeks premature. Breech presentation and the child suffered second degree asphyxia. Birth weight 2500 g. In the neonatal period there was flaccidity and cyanosis and at the same time a rapid increase in head circumference. Ratio at three months was 0.70/0.67, third ventricle 13 mm. The choroid plexus on the left side was coagulated but as the head continued to increase in size craniotomy was performed on the right side and a purulent meningitis was found. He remained in a paediatric ward until he died at the age of 10 months.

Autopsy: the lungs showed basal atelectasis. Brain: meninges and cerebrum were adherent in the left occipital region, and there was severe dilatation of the lateral ventricles on both sides with marked atrophy of the cortex. In the right occipital region thin purulent fluid was found. Autopsy diagnosis: severe degree of internal hydrocephalus. Atrophy of the cortex. Localised purulent meningitis. Bilateral atelectasis of the lower lobes of the lungs.

Conclusion: birth injury with disturbance of the cerebrospinal fluid circulation and subsequent infection would account for the findings. It was not possible to comment on any possible prenatal influence.

Case no. 153

Clinical summary: girl who at the age of two years was unconscious for 3 hours after a fall and had convulsions. There were no further symptoms until she was 10 years old when she developed petit mal and had localised seizures of the right hand. V.E.G. performed when she was 14 years old showed a ratio of 0.29/0.31, third ventricle 3 mm. Left side - 10 mm. Later arteriography showed a possible atrophic lesion in the left hemisphere frontally. Operation revealed an old fracture. In the neighbourhood of Broca's centre was a typical atrophic lesion which was removed. Repeated S.E.G. at 23 years of age showed a ratio of 0.28/0.34, third ventricle 5 mm. Left side - 15 mm. In the following year she had an increasing number of seizures though no details are known. When she was 33 she was brought to the Casualty Department and was dead on arrival following a period of respiratory difficulty.

Autopsy: the marks of arteriographies could be seen in the neck, and both carotid arteries were narrowed and obliterated. Brain autopsy: meninges normal. Superficially there was a scar-like area on the left side in the area between the frontal and temporal lobe. A few small haemorrhages were present but no large ones. The vessels of the brain were normal. Microscopy of the pituitary was normal. Autopsy diagnosis: epilepsy. Sequelae of thorotrast injection. Partial pulmonary collapse and bronchitis. Hepatic cirrhosis. Hyperplasia of the spleen. Cholelithiasis.

Conclusion: postnatal trauma was a definite factor and could account for the findings as well as the course of the disease.

Case no. 181

Clinical summary: a girl whose birth was prolonged and difficult, and who had asphyxia. Following this she had attacks of opisthotonus five to ten times a day and showed no interest in her surroundings. V.E.G. at 1 year 9 months showed a ratio of 0.52/0.53, third ventricle large but not measurable. Right side - 6 mm. Increased amount of cortical air present. The child died three months later after admission to a medical ward because of general debility, vomiting, dehydration and a high temperature.

Autopsy: in the trachea and main bronchi was a small amount of yellow secretion. No signs of lung inflammation. Brain autopsy: on opening the cranium a large amount of liquor was found and the brain was atrophic, especially in the right frontal area. Gyri were small. The brain surface was irregular with large sunken areas. Cerebellum appeared normal. After fixation the brain was small, and the gyri were of normal size in only a few places and were mostly small and sunken. There was considerable dilatation of the ventricular system with pronounced atrophy of the dorsal areas. Occipitally the dilatation involved the left side. Pons and medulla normal. No definite sequelae from haemorrhage was found in the meninges or brain. Autopsy diagnosis: cerebral atrophy. Aspiration of stomach contents. Internal and external hydrocephalus.

Conclusion: haemorrhage as a result of birth injury and disturbance of the cerebrospinal fluid circulation leading to dilatation and atrophy would explain the findings. The patient died of hyperpyrexia of unknown origin.

Case no. 216

Clinical summary: a girl whose mother bled for three days during the fourth and fifth months of pregnancy and also vomited. Delivery was difficult. The second stage lasted some hours. Birth weight 3000 g. Slight jaundice was present. At six months trembling of the head and hands was noticed and development was slow. She was admitted on several occasions with a diagnosis of possible ataxia. L.E.G. was normal. At two years of age V.E.G. showed a ratio of 0.28/0.35, third ventricle 11 mm. Biopsy of the cortex showed severe degeneration of the ganglion cells and possible congenital dysplasia. Shortly after this she was again admitted to a paediatric ward where she had continuous fibrillations and frequently ran a high temperature. She died at two years and eleven months of age.

Autopsy: lungs hyperaemic and oedematous with scattered small consolidations, particularly in the right lower lobe. Trachea and main bronchi contained mucopus and the mucous membranes were swollen and injected. Liver and spleen enlarged. Brain autopsy: marked oedema and injection of the meninges. On sectioning, the brain showed generalised injection with no other macroscopic changes. The ependyma at the base of the fourth ventricle was injected. Posteriorly in the cranium burr holes due to V.E.G. were found. Microscopy of the brain tissue showed stasis and oedema. Structure was normal elsewhere with no abnormal cell infiltrations. Stasis and oedema most pronounced in the meninges. Autopsy diagnosis: cerebral oedema. Acute tracheobronchitis. Pulmonary hyperaemia and oedema. Patchy bronchopneumonia. Degeneration of liver and acute hyperplasia of spleen. Sequelae of ventriculography.

Conclusion: from the case history there were several possibilities to be considered, of which perinatal damage was thought to be the most likely. It was impossible to evaluate the influence of prenatal factors or the jaundice. The trembling could have been due to a disorder in the basal ganglia or to a cerebellar condition.

Case no. 271

Clinical summary: a girl born two months prematurely. Birth weight 1700 g. Delivery was precipitate and there was prolapse of the cord. The child was blue and flaccid. She was admitted to the local hospital for five to six weeks. After discharge she had stomach trouble and was re-admitted. She was dehydrated, had convulsions and was opisthotonic. Admitted to the neurosurgical ward at two months of age, and V.E.G. showed a ratio of 0.73/0.60, third ventricle 10 mm. Right side - 5 mm. There was a markedly increased distance between the lateral ventricles such as seen in cases of non-communicating cysts of the septum pellucidum. She was admitted to a State Institution at six months of age and remained there until she died five months later. The head circumference had increased during admission from 54 cms. to 64 cms. Her condition deteriorated and she had frequent febrile episodes. She died apparently from bronchitis and aspiration pneumonia with a temperature of 40° C.

Autopsy: the trachea and bronchi contained stomach contents. In the lungs a number of sunken areas about 3 cms. in size were found but no definite pneumonic changes. Brain autopsy: cranium was large, 64 cms., and the bones were paper thin. Anterior fontanelle measured 12 cms. Enlargement was symmetrical. On sectioning, the ventricles were perforated and two litres of clear fluid escaped. The amount of sub-arachnoid fluid was small and no adhesions or signs of earlier meningitis were present. The enormously dilated brain was pressed close to the cranial bones so that the gyri were very broad and sulci narrowed. Fourth ventricle was not dilated. The medial and lateral foramina were free. It was not possible to pass through the cerebral aqueduct of Sylvius. Third and lateral ventricles enormously dilated. Brain tissue measured only a few millimetres. The basal surface of the cerebellum revealed pronounced cone formation but was not pressed down in the foramen magnum. No sinus thrombosis was found. Autopsy diagnosis: stenosis of Sylvian aqueduct. Severe internal hydrocephalus. Capillary bronchitis. Diffuse pulmonary atelectasis and obstruction. Aspiration of stomach contents.

Conclusion: the P.E.G. findings corresponded with the autopsy results. The aetiological factors were complicated by prematurity, perinatal complications with cyanosis and flaccidity, and the marked dehydration and poor general condition when only a few weeks old. All could be held responsible.

In the following 13 autopsied cases, examination of the brain as well as most of the general autopsies were carried out at the Rigshospital.

Case no. 33

Clinical summary: a boy with a family history of a blood disorder and splenectomy in several members. Birth was six weeks premature. Birth weight 1850 g. He was admitted immediately to the paediatric ward because of alternating flaccidity and rigidity. There was jaundice from the third day until one month of age. After doing well for a while he again became rigid with a tendency to opisthotonus and cyanosis. V.E.G. at five months of age showed a ratio of 0.29/0.32, third ventricle 4 mm. Admitted to a State Institution at two years of age and died the day after admission in hyperpyrexia.

Autopsy: pulmonary stasis and oedema. Acute emphysema. Acute stasis of the organs. Petechiae of the thymus, pericardium and pleura. Hypertrophy of the left tonsil. Enlarged oesophagus. Brain autopsy: head circumference 45.5 cm. The brain gave the impression of being heavier than normal. Pronounced saturation of the brain tissue with blood and fluid was present as well as stasis in the innermost leptomeninges. The cavities of the brain were slightly dilated. Convulsions were flattened. No signs of trauma or bleeding could be found. Fluid was clear. No areas of destruction or cyst formation. The brain weight was unfortunately not recorded.

Microscopy: moderate oedema of the leptomeninges with no signs of infection. The cortical layers are well-differentiated but there is a lack of ganglion cell layers so that although one can find cells they are few and most are poorly developed, oedematous

and degenerated. In between are a few normal ganglion cells. Myelination is good. The changes in the ganglion cells are most pronounced anteriorly and the oedema of the cortex and meninges posteriorly. The sections from the basal ganglia show defects of myelination and a marked tendency to necrosis and cavitation localised to the anterior part of the globus pallidus. There is no tissue reaction in this area. These changes cannot be seen in any other part of the basal ganglia nor is the internal capsule affected. The ependyma of the ventricles is normal. Hyperaemia is more marked in the hypothalamus and here perivascular haemorrhages and slight perivascular infiltration of lymphocytes and monocytes are present. Brain autopsy diagnosis: congenital cerebral dysplasia. Status dysmyelinatus (globus pallidus). Cerebral hyperaemia and oedema. Hypothalamic encephalitis.

Conclusion: the changes of the globus pallidus and hypothalamus could be the sequelae of kernicterus following prematurity and possibly the familial blood disorder. The involvement of the hypothalamus could explain the marked rise of temperature. The slight dilatation of the cavities corresponded well to the P.E.G. findings.

Case no. 96

Clinical summary: boy whose paternal aunt was oligophrenic. The mother had hypertension during pregnancy. Delivery was uncomplicated. Symptoms occurred from the age of two years with increasing gait difficulties and speech disturbance. V.E.G. when three years old showed a ratio of 0.36/0.35, third ventricle 3 mm. The disorder progressed over the next few years and later L.E.G. showed ratios of 0.36/0.38. The child died suddenly during a stay in a treatment home when he was ten years old.

Autopsy: in general nothing abnormal was found. Brain: macroscopically normal. At coronal section slight dilatation of the ventricular system was found (Fig. 40).

Microscopy: shows symmetrical changes of the basal ganglia especially of the caudate nuclei and putamen, less pronounced in the globus pallidus. In addition, changes are present in the medulla and spinal cord. The changes are at different stages so that the most caudally placed are the latest to appear. The oldest changes consist of cystic degeneration and gliosis, the most recent of hyperaemia, nerve cell degeneration and degeneration of the white matter and reticular formation. Autopsy diagnosis: status dysmyelinatus (nucleus caudatus, putamen and globus pallidus). Hyperaemia and oedema of the medulla and spinal cord.

Conclusion: this case is discussed in detail in a special report. It was not possible to find a corresponding clinical picture of torsion spasms and rigidity showing the same pathological changes localised chiefly to the paleo striatum. With regard to the P.E.G. changes and biopsy findings, there was a close correlation. Moderate dilatation was found with atrophy of the caudate nuclei in particular. Repeated P.E.G.'s revealed no remarkable increase in ratio but clear alteration in the structure of the lateral border. This was an example of progression which could not be measured by means of ratio but where a more specific description was needed. Measurement of the distance between the septum pellucidum and medial limit of the caudate nuclei (Troland *et al.*, Engeset) would not give very helpful figures because the normal increase in size in the interval from three to ten years of age would largely explain a difference or, in any case, make the exact difference uncertain.

Case no. 112

Clinical summary: girl whose mother had a narrow pelvis though delivery itself was uncomplicated. At the age of seven months the child developed a cold and otitis media, and following convulsions a diagnosis of encephalitis was made. Lumbar puncture was normal. As development ceased L.E.G. was performed. Ratio was 0.39/0.34, third ventricle 12 mm. There was an abnormal amount of cortical air in the frontal area. At the age of eighteen months operation was performed on both sides of the cranium, and this revealed thick membranes in both hemispheres and on the right side fluid was present between the membranes. On the left side there was cerebrospinal fluid under the arachnoid membrane. Microscopy showed outer and inner membrane from sub-dural

haematoma. Subsequent course was characterised by lack of development, rigidity and microcephaly. She died when six years old.

Autopsy: tracheo-bronchitis and muco-purulent bronchiolitis were found with acute stasis and hyperaemia of the organs. Brain autopsy: weight 300 g. Diffuse atrophy and microgyri (Fig. 41). Cerebellum and brain stem normal. On the convexity and at the base of the brain there were reddish-grey sub-dural membranes and the dura was fibrosed and thickened. No pronounced thickening of the leptomeninges. On frontal section of the brain there was diffuse ventricular dilatation (Fig. 42). Anterior horns measured 16 mm. diagonally and 13 mm. transversely. Third ventricle at its widest point was 7 mm. Gyri were small and atrophic, and the sulci broad and deep. No destruction or haemorrhage present.

Microscopy: covering all the dural sections there is a thick membrane on the inner side without signs of inflammation, whereas in several places there are perivascular haemorrhages of different ages, and in a few places early bone metaplasia. Severe degenerative changes are present in the cortex but in the best preserved areas normal layer differentiation can be found, also normally developed and preserved ganglion cells. Myelination is incomplete in the white matter. There is marked widespread glial proliferation. In the striate bodies the ganglion cells are relatively well-preserved and myelination is fairly good. No inflammatory changes are present. Good myelination is present in the brain stem except in the area corresponding to the pyramidal tracts. Diagnosis: microcephaly and microgyria with bilateral sub-dural haematoma.

Conclusion: in spite of negative information on birth complications, it must be assumed that there was a sub-dural haemorrhage, possibly due to the mother's narrow pelvis. The most likely explanation of the acute episode at seven months of age was that it corresponded to an acute change in the sub-dural haematoma with disturbed colloid-osmotic conditions and effusion as described by Christensen 1941. Another possibility could be an infection in an existing haematoma but in this case one would have expected to find signs of this at operation or at autopsy. A further possibility is that the infection precipitated destruction in a sub-dural haematoma. The ventricular system was found to be moderately dilated. Exact measurements could hardly be applied as the brain was so small.

Case no. 121

Clinical summary: boy born three weeks prematurely after a pregnancy complicated by hypertension and eclampsia. Birth weight 2100 g. Gastro-enteritis developed immediately after delivery and following this development was retarded. This was noticed at ten months to be particularly marked on the left side of the body. After S.E.G. at sixteen months which showed a ratio of 0.37/0.42 and a third ventricle of 11 mm., burr holes were performed and clear fluid found on both sides with thickened arachnoid membrane. The patient was semi-conscious most of the time and died shortly after the examination (see p. 80).

Autopsy: hyperaemia and oedema of the brain with flattened gyri but no cone formation. Brain was severely damaged during removal. Only moderate ventricular dilatation was found. Macroscopic examination showed normal structure of pons and cerebellum while the medulla looked somewhat altered. The only tissue which could be microscopically examined was the medulla which was normal except for slight hyperaemia. Autopsy diagnosis: cerebral hyperaemia.

Conclusion: autopsy did not throw any light on the cause of death. The hyperaemia which also involved the medulla led one to think of a brain stem condition. The moderate ventricular dilatation corresponded well to the ratio and the large third ventricle fitted in with the possibility of a centrally placed lesion.

Case no. 135

Clinical summary: boy born three weeks prematurely. Birth weight 3750 g. He was asphyxiated and flaccid during the first few days. He failed to gain weight and was retarded in development, particularly motor development. L.E.G. ratio was 0.44/0.45,

third ventricle 9 mm. Two days after his admission to an institution he developed a temperature of 41.2° C. and died in a state of shock.

Autopsy: macroscopically normal findings. Microscopy shows hyperaemia of the liver tissue and changes of Kimmelstiel-Wilson's type in the glomeruli of the kidneys. Brain weight after fixation 1100 g. Brain is oedematous with cone formation and hyperaemia of the pia vessels. Only moderate ventricular dilatation is present and no particular dilatation of the fourth ventricle.

Microscopy shows oedema and post-mortem decomposition of all sections. Meninges slightly oedematous and hyperaemic. No real differentiation between the layers of the cortex but evaluation is difficult due to the oedema. Ganglion cells and cortex look immature in several places but the white matter is well-developed and the myelin sheaths are well-preserved even if a few are swollen. In the basal ganglia immaturity of the ganglion cells is present. Pons, cerebellum and medulla are normal. Autopsy diagnosis: severe cerebral oedema. Congenital cerebral dysplasia. Post-mortem decomposition. Slight hydrocephalus.

Conclusion: the ventricular system as described at autopsy was even smaller than on X-ray examination but this can be explained by the presence of oedema and post-mortem decomposition which might have reduced the size of the cavities. The aetiology was uncertain. An early damage was possible but whether this was due to prenatal or perinatal factors was not certain.

Case no. 139

Clinical summary: boy whose delivery was induced medically and who, in the first twenty-four hours, had trembling and shortly afterwards convulsions of the arms. S.E.G. at nine months revealed a ratio of 0.41/0.41 and a third ventricle of 13 mm. V.E.G. ten days later revealed a ratio of 0.46/0.45 and a third ventricle of 14 mm. His condition continued to be poor and he was admitted to an institution at nineteen months. He died shortly afterwards in hyperpyrexia, possibly due to influenza.

Autopsy: acute bronchitis. Partial collapse of the lungs and compensating pulmonary emphysema. Hypertrophy of the spleen. Brain autopsy: weight after fixation 400 g. Microcephaly and irregular gyrus formation with both macro- and microgyri. There were a great number of sunken areas corresponding to the under-developed gyri, and here there were sub-arachnoid fluid collections. Pons, cerebellum and medulla also gave the impression of being underdeveloped. On frontal section marked ventricular dilatation was found, including the aqueduct and the fourth ventricle. Third ventricle at its widest point measured 13 mm. There was diffuse atrophy of the white matter as well as the basal ganglia.

Microscopy: there are varying degrees of laminal necrosis in the cortex especially the third and fifth ganglion cell layers. In addition there is proliferation of the vessels and astrocytes. There is sub-pial glial proliferation and the white matter is poorly developed. In the basal ganglia glial proliferation is present and in the white matter the myelinated neurofibrils are separated and poorly stained but nowhere is there complete degeneration. Autopsy diagnosis: progressive polio- and leucodystrophy following cerebral anoxia.

Conclusion: birth trauma anoxia was likely but prenatal damage cannot be excluded. There was good correlation between P.E.G. findings and autopsy findings.

Case no. 170

Clinical summary: boy whose mother had pyuria during pregnancy and who suffered from convulsions at the age of three months. S.E.G. at the age of five months showed a ratio of 0.36/0.33, third ventricle impossible to measure. Right side - 13 mm. A great deal of cortical air was found on the left side. As the seizures were thought to be hypoglycaemic an exploratory laparotomy was performed but no insulinoma was found. At V.E.G. at eight months the ratio was 0.36/0.38, third ventricle 9 mm. Left side - 7 mm. On this occasion an abnormal amount of cortical air was found over the right hemisphere. Patient died two months later and autopsy revealed bronchopneumonia and empyema.

Brain autopsy: weight after fixation 650 g. A few gyri in the frontal area and close to the right central sulcus were shrunken but otherwise there were no signs of cortical atrophy. There was moderate dilatation of the anterior horns and the third ventricle. In the pituitary fossa there was bulging of the third ventricle above the optic chiasma.

Microscopy: no signs of infection present. In the cortex layer differentiation is not complete and the ganglion cells are immature. There is no glial proliferation or degenerative ganglion cell changes. Basal ganglia and hypothalamus are normal. There is early myelination of the white matter. Diagnosis: slight internal hydrocephalus; cerebral oedema and hyperaemia. Brain of a premature infant with delayed development.

Conclusion: as stated in the report on this patient, there was disagreement between the P.E.G. and autopsy findings, but not to any great degree if one maintains the requirement that it must be possible to reproduce cortical air changes on repeated P.E.G.'s. If this was the case, the respective findings on the right and left would make one doubt their validity. For this reason the patient was not included in the present group of cortical findings. It is, nevertheless, correct to say that the age factor played an important part, particularly in connection with the variability of the sub-arachnoid space in infants. The hypoglycaemic seizures were presumably of cerebral origin.

Case no. 183

Clinical summary: girl with a familial predisposition to oligophrenia. At four months of age she sustained a head injury and at eight months developed convulsions. Following this, development was retarded. S.E.G. at 2½ years showed a ratio of 0.62/64, third ventricle impossible to measure. Right side - 5 mm. E.E.G: a focus was found anteriorly on the left side. Operation at this site showed firm sub-dural adhesions and a circumscribed atrophic lesion with microgyri. When this was removed several small sub-cortical cysts were found. After operation it was found that the enormously dilated ventricular system had collapsed on the left side. The day following operation the patient went into shock and died.

Autopsy: the brain had collapsed during fixation. An operation cavity was found in the left pre-motor region measuring 2×3.5 cm. This cavity extended into the dilated anterior horn. There were microgyri in both pre-motor regions and occipital regions, and on cut sections polyporencephaly was found on the right side but not on the left. The posterior horn was so dilated that the brain tissue measured only a few millimetres. The remainder of the ventricular system was unequally dilated, the anterior horns moderately and the temporal horns slightly. Third ventricle was slightly dilated and the fourth ventricle was normal. Basal ganglia, pons, medulla and cerebellum appeared normal.

Microscopy: in the right occipital lobe porencephalic processes are present and there is no normal layer differentiation. Immature ganglion cells are seen with insufficient pigmentation. The gyri are atrophic and the cyst walls are made up of glial tissue. There is no myelination. In sections from the left occipital region very thin cortical tissue is found. The inner side is to some extent covered by ependyma and there is no normal cortical structure. The same changes but less pronounced are found frontally, and here there is a great amount of blood pigmentation present, some of which is in macrophages. Diagnosis: localised microgyria with cortical atrophy. Polyporencephaly and sequelae of cerebral haemorrhage. Severe internal hydrocephalus.

Conclusion: there was definite correlation between the P.E.G. findings and autopsy. It was not possible to say definitely when the disease started but a case can be made out for a pre- or perinatal aetiology. At the same time all the changes could be acquired postnatally (Benda and Hoessly 1956).

Case no. 217

Clinical summary: boy whose mother suffered from vomiting during pregnancy and had influenza during the sixth month. The patient began to have infantile spasms at four months and following this appeared to be very retarded. V.E.G. at six months of age showed a ratio of 0.34/0.44. Third ventricle 11 mm. His condition deteriorated

and he was admitted when two years old to a paediatric ward with a high fever which was thought to be due to pneumonia but autopsy did not confirm this.

Autopsy: brain autopsy revealed a large cyst in the left hemisphere centred around the Sylvian fissure (Fig. 43). During removal fluid escaped. The brain weighed 855 g. and its surface was normal as far as gyri and sulci were concerned apart from the cyst. No changes were found in the vessels. The cyst extended from the base of the left frontal lobe and included the tissue in the lateral ventricle's ependyma. The basal ganglia on the left side showed cystic changes. No communication with the ventricular system could be found. On cut sections a cyst was found on the right side in the head of the caudate nucleus and putamen, but otherwise no macroscopic changes were present in the basal ganglia (Fig. 44).

Microscopy: the cyst walls and trabecular areas consist of fibrillar astrocytes and in the periphery perivascular encephalomalacia is present, also lipid-containing macrophages. On the ventricular walls adjacent to the cyst granular ependymitis is present. There is normal layer differentiation in the cortex but the ganglion and glial cells look pyknotic and show varying degrees of atrophy. In the cerebellum the Purkinje cells are atrophic. The brain stem is normal. Autopsy diagnosis: polyporencephaly. Sequelae of cerebral anoxia. Cortical atrophy of brain and cerebellum. Internal hydrocephalus.

Conclusion: the dilatation shown on P.E.G. corresponds to the findings at autopsy. The polyporencephalies were not found to communicate with the ventricular system and this explains why they cannot be seen. Presumably the damage occurred late in pregnancy or during delivery. The patient displayed the clinical picture of infantile spasms and the E.E.G. showed hypsarrhythmia.

Case no. 226

Clinical summary: a boy who had slight jaundice for the first two weeks of life. At the age of five months he had generalised convulsions. S.E.G. at six months showed a ratio of 0.50/0.43, third ventricle 10 mm. At the age of two and a half he was admitted to a State Institution and his condition deteriorated. There were frequent convulsions and an increasing number of athetoid movements. Three months after admission he developed a high temperature and pneumonia and died in spite of intensive antibiotic therapy.

Autopsy: brain weighed 400 g. after fixation. Marked microcephaly. In several places, especially over the frontal lobes, sub-arachnoid fluid collections were found. The leptomeninges showed some fibrosis. There was diffuse moderate and severe dilatation of the ventricular system including the aqueduct and fourth ventricle. There was atrophy of the grey matter of the cortex and in the basal ganglia as well as the corona radiata. There was no clear demarcation between the different tissues in the basal ganglia macroscopically. Third ventricle measured 10 mm. Pons, cerebellum and medulla were smaller than usual but otherwise appeared normal.

Microscopy: no cell layer differentiation is seen in the cortex. There are only a few ganglion cells and most of these are atrophied. There is pronounced glial proliferation. Below the second layer the consistency is almost spongy and a laminal necrosis is found corresponding to the third and fifth layers. Microscopically the basal ganglia show poor differentiation between the different parts. Cerebellum is normal. The pons and medulla show some glial proliferation. The leptomeninges are slightly thickened corresponding to the temporal lobes. The myelin sheaths are slightly degenerated. Diagnosis: progressive polio-dystrophy of the brain following cerebral anoxia.

Conclusion: the pathological picture, especially the cortical changes, corresponds to sequelae of anoxia. The findings in the basal ganglia could be due to this or possibly to the jaundice. There was close correlation between the P.E.G. and autopsy findings.

Case no. 231

Clinical summary: a boy who had a difficult forceps delivery. He was asphyxiated for 45 minutes. During the first month he was frequently cyanotic and semi-conscious. He was admitted at five months to a State Institution. Investigation in the Paediatric Department

because of loss of weight and vomiting revealed a hiatus hernia. V.E.G. performed at eleven months showed a ratio of 0.70/0.81. Third ventricle was very dilated but exact measurement was not possible. Sub-dural air was present especially on the right side. Cortical biopsy showed slight meningeal reaction. He died shortly after discharge with fever which resisted all antibiotic therapy.

Autopsy: the brain collapsed on removal. Weight after fixation 340 g. Pronounced microgyri were present around the fissure Rolandi and posteriorly. Thrombosis was found in the vessels surrounding the left Sylvian fissure. Absence of corpus callosum. Scattered over the whole brain were porencephalic processes. Cerebellum appeared least affected and porencephalic processes appeared to be of earlier origin than in the cerebrum.

Microscopy: the differentiation of the cortical layers is not complete. The ganglion cells appear immature and glial proliferation is present. Myelination is less pronounced than usual. There is oedema of the meninges but no sign of infection. In several places lipid-containing macrophages are present. Around the porencephalic processes glial reaction can be seen and at some distance infiltration of lymphocytes. In the cerebellum there are some areas with possible early destruction but no real cavity formation. The vessel from the left Sylvian fissure shows thrombosis. Diagnosis: polyporencephaly and internal hydrocephalus (sequelae of cerebral anoxia). Thrombophlebitis of left Sylvian fissure.

Conclusion: there was good correlation between the clinical findings, aetiology, P.E.G. and autopsy findings, all of which corresponded to sequelae of birth anoxia of long duration. The findings supported the idea of vascular pathogenesis in a number of these cases as suggested by Christensen and Schondel (1946) and Benda (1952) among others.

Case no. 257

Clinical summary: boy born three weeks prematurely. Birth weight 2200 g. Cried a lot from birth. When four months old bilateral cataract and microcephaly were found. He was retarded mentally and physically. From the age of one year he had convulsions and V.E.G. was performed at eighteen months. Ratio was 0.46/0.38, third ventricle 5 mm. Right side - 11 mm. Admitted to a State Institution when he was almost two years of age and died a few days before his fourth birthday. He had a high fever for a few days and tonsillitis and bronchopneumonia were diagnosed.

Autopsy: brain weight after fixation was 1000 g. It was damaged on removal and therefore exact measurements were not possible.

Microscopy: cell layer differentiation is incomplete and the ganglion cells are underdeveloped. There is marked proliferation of oligodendroglia and astrocytes. There is no sign of infection or vessel changes. Leptomeninges normal. Thalamus, hypothalamus, cerebellum and medulla are normal. Diagnosis: congenital cerebral dysplasia. Cerebral gliosis.

Conclusion: prenatal damage in the form of an infection leading to cerebral dysplasia and cataracts was the most likely possibility. Unfortunately it was not possible to establish the relationship between the ventricular system as seen on P.E.G. and at autopsy, but there must have been fairly pronounced dilatation.

Case no. 268

Clinical summary: girl whose birth was normal but who did not cry until four hours after delivery. At thirty-six hours she had convulsions. Lumbar puncture showed straw-coloured fluid with elevated protein content. Development had been very much retarded and characterised by rigidity especially of the limbs on the left side. V.E.G. when one year old showed a ratio of 0.46/0.66, third ventricle 12 mm. Left side - 12 mm. There was increased cortical air on both sides. Microscopy of biopsy material showed proliferated inner capillary membrane (? stasis, ? membrane). She was admitted to a State Institution and died at two years five months after being ill for several weeks with continuous convulsions.

Autopsy: brain weight after fixation 660 g. Brain was smaller than normal (Fig. 45). There were diffuse, somewhat unequal microgyri. On the under surface of the right

frontal lobe the gyri were flattened due to severe dilatation of the anterior horn. No definite thickening of the leptomeninges was found. Cerebellum looked normal. On frontal section the brain tissue appeared spongy with cavities of different size, most pronounced in the anterior two-thirds. The ventricles were very much dilated and the right anterior horn was surrounded by small cavities which appeared to communicate (Fig. 46). The third ventricle was also dilated. The changes continued into the lateral part of the corpus striatum and thalamus. The internal capsule was only vaguely outlined. Aqueduct and fourth ventricle were not dilated.

Microscopy: there is oedema of the leptomeninges, but no fibrotic changes. In some parts of the cortex the layer differentiation is maintained but the ganglion cells appear degenerate. There are cystic cavities everywhere with glia trabeculation and pronounced glial proliferation. In several parts communication between the porencephalies and the ventricular system is seen. Scattered myelination can be seen but does not correspond with age. Sections from mesencephalon, pons, medulla and cerebellum show well-preserved structures. Diagnosis: severe polyporencephaly following cerebral anoxia.

Conclusion: the changes could be attributed to the anoxic period immediately after birth. The degree of dilatation of the ventricular system found at autopsy corresponded to the P.E.G. findings at which time the porencephalies were presumably non-communicating.

In conclusion concerning autopsy results, a close correlation was found to exist between P.E.G. and autopsy findings and in no case did the P.E.G. show findings which could not be confirmed at autopsy.

As might be expected, the autopsies included a great number of organic brain damages with almost complete destruction of normal tissue, and in particular perinatal damage with porencephalic formation. One obtains the impression that in the age group in which most of the children died, it was primarily a question of time of onset of the disorder rather than cause. It was, for instance, comparable to the problem of infantile spasms and to the pathological findings in demyelinating disorders in children. Furthermore, as a result of clinical experience in the present work, where the time factor has been of definite importance, the immature central nervous system appeared to be more vulnerable than a more mature one because in the latter the damage was more likely to be localised.

Autopsy findings, other pathological examinations as well as repeated P.E.G.'s confirmed that the findings seen on P.E.G. were real and were not dependent on a number of external factors.

Summary

Chapter I: the purpose of the present study is to examine the prognostic value of pneumoencephalography in a number of childhood disorders causing either real or apparent dilatation of the ventricular system. The value of certain measuring methods is examined and the reliability of one such method is ascertained.

Chapter II: a survey of the literature on pneumoencephalography is made, and this is divided into four parts. The first reviews its development with special reference to experimental examinations, results and complications in adults. In the second part reports concerning paediatric examinations are mentioned, and in the third the development of P.E.G. in Denmark is briefly reviewed. The picture revealed is that of a tendency for interest to fluctuate over the 40 years. At the beginning excessive enthusiasm was resisted strongly. In the next ten years there was little critical evaluation of the examination but this was followed by increasing interest in factors influencing complications. In the last ten years the use of air insufflation has increased, in other fields as well as in tumour diagnosis and there has been a more critical evaluation of the results obtained. In the fourth section the different measurements which are used to evaluate the degree of dilatation of the ventricular system are discussed. These methods are divided into planimetric and linear measurements and are given as exact or relative values. The P.E.G. measurements in suitable cases can be compared with autopsy material. The most frequently used figures are Evans' ratio and Schiersmann's index and these are discussed in detail, and it is emphasised that the use of relative values are of particular importance in childhood where the exact figures vary very much.

Chapter III: this chapter begins by discussing terminology and abbreviations used in the text. The present material is made up of 271 children (171 boys and 100 girls). To be included in the material the following criteria had to be fulfilled:

- (i) All patients were under fifteen years of age at the time of examination in the Neurosurgical Department.
- (ii) Tumours and acute infections of the C.N.S. were excluded.
- (iii) P.E.G. was performed either in the Neurosurgical Department or immediately before admission.

- (iv) At least one lateral ventricle on P.E.G. was greater than a quarter of the distance from the ventricular system's midline to the internal cranial wall (a ratio of 0.25 or more).
- (v) Admission was before July 1955 and therefore the shortest observation period was a year.

At the time of admission 74 children were less than a year old and 126 less than two years. The symptoms fell mainly into three groups: (a) Motor handicap, (b) Mental retardation and (c) Convulsions. In 158 patients the disease was recognised before the age of one year. As far as aetiological factors are concerned, familial predisposition accounts for 10%, prenatal damage for 15%, perinatal damage for 40% and postnatal factors for approximately 40%. About 40% of the cases suggest multiple aetiology.

The evaluation of P.E.G. is only attempted when there is adequate filling of the ventricular system. The internal cranial width and the greatest width of the anterior horns are measured and from this Evans' ratio is calculated. The same measurement is performed on each side and a ratio obtained for the right and left side. At the same time information on possible displacement of the ventricular system's midline is obtained. The width of the third ventricle is measured and the amount of cortical air assessed but no exact measurement is made. Finally, findings of special significance are reported.

As a result of these measurements the material is divided into five major types of ventricular dilatation:

- (a) Bilateral dilatation with equal ratios without displacement.
- (b) Bilateral dilatation with equal ratios with at least 5 mm. displacement.
- (c) Bilateral dilatation with different ratios on each side but without displacement.
- (d) Bilateral dilatation with different ratios on each side with displacement. The difference in ratio has to be more than 0.05 before being considered significant.
- (e) This group is made up of few patients and consists of those with only one lateral ventricle ratio of 0.25 or more.

More than 50% are in the first group where the dilatation is almost symmetrical.

The left lateral ventricle is more frequently dilated than the right. The third ventricle varies in size from 2-26 mm.

A febrile episode of a few days' duration is present in approximately 70% of the children after insufflation. More serious complications such as latent or manifest shock, marked neck and back stiffness etc. are present in only a few. Two deaths occur within twenty-four hours of insufflation. Both children have relatively large third ventricles but only moderate dilatation of the lateral ventricles. The mortality rate is low especially when one considers the number

of children included in the material who are already very ill at the time of the examination (58 of the 271 patients had died at the time of follow-up).

Finally, mention is made of the skull X-rays and electroencephalography.

Chapter IV: the follow-up examination includes all 271 patients, and most of them were personally examined by the author. The patient's condition is assessed from two standpoints: (1) Evaluation of the patient's condition at the time of follow-up, i.e. whether he is healthy, has symptoms, or whether he is under institutional care or dead and (2) An evaluation based on the changes which have taken place in the patient's condition between the time of admission and the time of follow-up. In this latter category the findings are classified as improved, unchanged or worse.

Independent of the method of evaluation, it is shown that as far as the degree of dilatation of the ventricular system is concerned, the results as expressed in terms of ratio are the same. The smaller the ratio is, the better the prognosis. In the group with a ratio under 0.30 approximately 80% have done well, and in the group with a ratio of 0.50 or more, more than 80% are under care or have died.

It is shown that it makes little difference whether Evans' ratio or Schiersmann's index is used but the former method is superior in cases of displacement of the ventricular system or unequal ratio.

Unilateral dilatations have a better prognosis than other types.

If the ratios are unequal the prognosis is dependent on the ratio difference and the total degree of dilatation.

The presence of cortical air in great amounts has serious prognostic implications, but is better if the air is frontally placed compared to any other position. Bilateral changes have the worst prognosis, and this is also the case in children below one year of age, so that one cannot consider changes in this age group as merely accidental.

The width of the third ventricle is of definite prognostic value. Only a few patients with a third ventricle width of more than 8 mm. have done well. With this measurement one uses exact figures and these are related to age and cranial diameter. Almost all patients who have done well have third ventricles below 6 mm. in diameter and cranial diameters greater than or corresponding to their age.

The period of observation has no bearing on the follow-up results.

The age at the time of examination shows a fairly uniform distribution of different types of P.E.G. The only specific finding in the older age groups is that there are not such severe degrees of dilatation. The age at the time of recognition of the disease seems to have a definite bearing on the prognosis. The later the disease is recognised, the better is the prognosis.

As might be expected, there is no definite relationship between symptoms and P.E.G. findings. In cases of mental retardation there is a correlation between the lower I.Q.'s and severe dilatation of the ventricular system.

The symptoms as well as their time of recognition are related to the follow-up results, and it is seen that the disorders which are recognised late, regardless of their character, have a better prognosis than those recognised earlier, with a definite dividing line at two years of age. This corresponds to the absence of high ratios in the older age groups.

The different aetiological factors are related to P.E.G. findings and to the follow-up examination. It is shown that patients with a familial predisposition have a somewhat worse prognosis than one would have expected from their ratios. The most severe changes and the poorest prognoses are linked with perinatal changes, whereas patients with postnatal damage frequently do well and often show asymmetrical and possibly unilateral dilatation.

Changes found on X-ray examination of the skull have no particular prognostic value. This is applicable to increased digital markings and deep posterior fossae. Changes in shape, however, often indicate a poor prognosis. This is true when the relationship between head circumference and prognosis is examined, but microcephaly is of much more serious prognostic value than macrocephaly.

E.E.G. shows the relationship between focal changes and non-symmetrical ventricular dilatation, but there is no particular relationship between cortical air findings and E.E.G. An abnormal E.E.G. under one year of age is a bad sign, whereas a normal E.E.G. in the same age group is not necessarily a good sign. Severely dilated third ventricles are most often associated with abnormal E.E.G.'s but not with a specific type.

Chapter V: this concerns 63 patients who have had more than one P.E.G. examination. This is considered an important method of evaluating the use of ratios. It is shown that there is a close correlation between the different P.E.G.'s. If the examinations are carried out within a short period of time there is almost no difference in the ratios obtained. If several years have elapsed the ratio is frequently the same even if there have been great changes in cranial diameter. In a number of cases the ratio has increased over the years, and this corresponds to a clinical deterioration. In no case is deterioration related to a diminishing dilatation. P.E.G.'s performed in other departments show the same close correlation and this means that by using relative figures the ratio becomes independent of technical factors, e.g. distance from the X-ray apparatus etc., whereas if exact figures are quoted, it is essential to have detailed information concerning such factors.

Chapter VI: operations performed and the results thereof are mentioned briefly. Good results are obtained in cases of removal of meningo-cerebral scars. Congenital malformations of various kinds and more severe perinatal damage do not show the same good results. Nevertheless, some patients have had cysts removed and have shown improvement.

Chapter VII: the pathological findings are discussed. The fact that cortical biopsies are often too small for detailed histological examination has in no case led one to suspect a more serious disorder which is not confirmed later.

The material obtained at operation confirms the cortical and sub-cortical findings but reveals little about the ventricular system.

The patients who have died are reported and it is shown that the direct causes of death are frequently febrile disorders, pneumonia or bronchitis or, in a great many cases, unknown but possibly cerebral hyperpyrexia. In this connection attention is drawn to the possibility of anxiety reactions precipitating "Voodoo deaths."

Autopsies have been carried out on 22 of the 58 patients who died, and these are discussed in detail. A close correlation is found between autopsy findings and P.E.G.'s.

Resumé

Kapitel I: Omtaler formålet med undersøgelsen. Det har været ønsket at undersøge den prognostiske værdi af PEG i barnealderen ved en række lidelser, der er kendetegnede ved formodet eller sikkert dilateret ventrikelsystem. Ydermere om en målemetode kunne benyttes dertil, samt hvor reproducerbare sådanne undersøgelser er.

Kapitel II: Her gennemgås litteraturen om pneumoencephalografi. Den er delt i 4 grupper. Først gives en oversigt over udviklingen i al almindelighed med specielt henblik på experimentelle undersøgelser, komplikationer og resultater i voksne materialer. Dernæst gennemgås de pædiatriske arbejder, og som 3. afsnit er udviklingen i Danmark kort gennemgået. Der er fællestræk for disse undersøgelser visende en bølgeformet bevægelse, begyndende med stor entusiasme og megen modstand i det første 10-år. I det følgende en ofte ukritisk anvendelse af undersøgelsen resulterende i udtalt reservation og mere vægt på undersøgelser af faktorer, der har indflydelse på komplikationerne. Det sidste 10-år viser påny stigende anvendelse af luftinsufflation også på andre områder end ved tumordiagnostiken, og de opnåede resultater bedømmes mere kritisk. Det sidste afsnit omtaler de hidtil anvendte målemetoder til vurdering af dilatation af ventrikelsystemet. Disse deles i: planimetri og lineære mål, der enten kan opgives som absolutte værdier eller angives som relative størrelser. Endnu en form for måling er undersøgelser på sektionsmaterialer og deres sammenligning med røntgenfundene. De to hyppigst anvendte metoder, Evans ratio og Schiersmanns index, omtales udførligt, idet det fremhæves, at netop anvendelse af relative værdier er af betydning i barnealderen, hvor absolutte størrelser varierer meget.

Kapitel III: Der gives en beskrivelse af de anvendte definitioner og forkortelser. Sammensætningen af det undersøgte patientmateriale gennemgås, materialet omfatter 271 børn (171 drenge og 100 piger). Følgende betingelser er opstillede for medtagelse i undersøgelsen: 1) Ptt. må ikke være fyldt 15 år ved undersøgelsen på neurokirurgisk afdeling. 2) Det må ikke dreje sig om tumor eller om en akut infektion af centralnervesystemet. 3) PEG er foretaget enten på afdelingen eller kort forinden. 4) Ved PEG er mindst een sideventrikel mere end 1/4 af afstanden til kranievæggen (dvs. ratio: 0.25 eller derover). 5) Indlæggelsen har fundet sted før 1/7 1955, således at den korteste observationstid er 1 år.

Ved indlæggelsen var 74 yngre end 1 år og 126 yngre end 2 år. Symptomerne faldt inden for 3 hovedgrupper: motorisk retardering, kramper og mental retardering. Hos 158 ptt. var lidelsen erkendt inden udgangen af 1. leveår. De ætiologiske muligheder var i ca. 10 % familiær disposition, 15 % prænatale skader, hos 40 % perinatale læsioner og i ca. 40 % postnatale faktorer. Ca. 40 % af sygehistorierne viste multiple ætiologiske faktorer.

Bedømmelsen af PEG er baseret på følgende forhold: Ventrikelsystemet skal være velfyldt. Den indvendige kraniebredde og største bredde af forhornene er målt, hvorefter Evans ratio udregnes. De samme målinger er gennemført for hver side for sig, således at man kan udregne en ratio for hver af siderne og samtidig få oplyst, om der er forskydning af ventrikelsystemets midtlinie. Bredden af 3. ventrikel er målt, og cortical luft er vurderet, uden at måling er gennemført her. Endelig anføres eventuelle specielle fund særskilt.

På grundlag af disse målinger kan materialet deles i 5 hovedtyper af ventrikulær dilatation: 1) dobbeltsidig dilatation med ens ratio uden eller 2) med forskydning, der er ansat til mindst 5 mm. Desuden kan dilatation have forskellige ratioer på de to sider og også her være 3) uden eller 4) med forskydning. En forskel i ratio er forlangt større end 0.05, førend den er anset for betydningsfuld. Den 5) gruppe er de ret få patienter, hvor kun een sideventrikel har en ratio svarende til 0,25 eller derover. Godt halvdelen af patienterne er i første gruppe, der kommer nærmest til begrebet symmetrisk dilatation. Venstre sideventrikel er langt hyppigere større end højre. 3. ventrikel varierer i størrelse fra 2 til 26 mm.

En febril periode efter PEG af et par dages varighed forekommer hos ca. 70 % af de undersøgte børn, hvorimod komplikationer af sværere art som latent eller manifest shock, udtalt nakke-rygstivhed o.l. kun forekommer i få tilfælde. Der er 2 dødsfald indenfor de første 24 timer efter undersøgelsen, begge børn med ret store 3. ventrikler, men i øvrigt med moderate dilatationer af ventrikelsystemet. Dette er ikke nogen høj mortalitet, specielt når man tager i betragtning, hvor mange dårlige børn der indgår i hele arbejdet (58 døde ved efterundersøgelsen af 271 ptt.)

Som afslutning omtales kort fundene ved røntgenundersøgelse af kraniet og elektroencephalografi.

Kapitel IV: Efterundersøgelsen omfatter alle 271 patienter, og langt de fleste er set af undersøgeren. Der redegøres for 2 hovedsynspunkter ved vurderingen af patienternes tilstand: 1) en placering efter deres absolutte tilstand, dvs. om de er raske, har symptomer af forskellig grad, er under forsorg eller er døde. 2) er en vurdering baseret på den forandring, der måtte være sket i deres tilstand mellem tidspunktet for indlæggelsen og efterundersøgelsen. Her udtrykkes fundene som bedrede, uforandrede eller værre.

Uanset hvilket synspunkt man anlægger, viser det sig, at sammenholdt med graden af dilatation af ventrikelsystemet udtrykt ved ratio, er der samme resultat: Jo mindre ratio jo bedre prognose. I gruppen med ratio under 0,30 er der

ca. 80 %, det er gået godt, og i gruppen med ratio 0,50 eller derover er mere end 80 % under forsorg eller døde.

Det er yderligere vist, at det ikke giver nogen forskel, om man anvender Evans ratio eller Schiersmann's index, men at den første er den bedste egnede i de tilfælde, hvor der er forskydning af ventrikelsystemet eller uens ratio.

De eensidige dilatationer har en bedre prognose end de øvrige typer. Hvis ratioerne er forskellige på de to sider, er den dårligste prognose knyttet til de største differencer og største samlede dilatationer.

Den corticale lufts tilstedeværelse i store mængder har en dårlig prognostisk indflydelse, dog er det knapt så udtalt, hvis luften er placeret frontalt som andre steder. Dårligst går det i de tilfælde, hvor der er dobbeltsidige forandringer. Dette gælder også mange børn under 1 år, således at man ikke kan anse forandringerne i denne aldersgruppe for tilfældige fund.

Bredden af 3. ventrikel er af afgørende prognostisk betydning. Kun få patienter med en 3. ventrikelbredde over 8 mm har klaret sig nogenlunde. Her anvendes absolutte mål, og disse er sat i relation til alder og kraniebredde. De patienter, der har klaret sig godt, har stort set alle haft 3. ventrikler under 6 mm i diameter og kraniediametre større end eller svarende til deres alder.

Observationstidens længde har ingen indflydelse på efterundersøgelsen. Alderen ved undersøgelsen viser ret ensartet fordeling af formerne for PEG, dog er der i de ældre aldersgrupper ingen meget svære dilatationer. Alderen ved sygdommens erkendelse viser sig at være af afgørende betydning for prognosen. Jo senere lidelsen er erkendt, jo bedre går det patienterne. Der er ingen sikker relation mellem de forskellige symptomer og PEG fundene. I tilfælde af mental retardering er der sammenhæng mellem lav IK og svær dilatation af ventrikelsystemet.

Såvel symptomer som tidspunktet for deres erkendelse er sat i relation til efterundersøgelsen, og det fremgår heraf, at ved de sent erkendte lidelser, uanset deres karakter, er prognosen bedre, end hvis de er erkendte før end 2 års alderen. Dette svarer til, at store ratioer ikke findes i de ældre grupper. De forskellige ætiologiske faktorer er sammenlignet med PEG fundene og efterundersøgelsen. Det viser sig, at patienter med familiær disposition har en relativt dårligere prognose end deres ratioer ville antyde. De sværeste forandringer og den dårligste prognose er knyttet til de perinatale forandringer, hvorimod de postnatale beskadigede ofte klarer sig ret godt. Ofte vil de postnatale forandringer være asymmetriske, eventuelt eensidige dilatationer.

De forandringer, der findes ved røntgenundersøgelse af kraniet, har ingen særlig betydning for prognosen, dette gælder således øgede impressiones og dybe, hængende fossae posteriores. Formforandringer af forskellig art har dog en ret dårlig prognose. Dette viser sig også at være tilfældet, når man undersøger sammenhængen mellem microcephali og prognose. For lille hovedomfang er et meget dårligt tegn, langt dårligere end for stort.

EEG viser overensstemmelse mellem focale forandringer og ikke-symmetriske ventrikelsystemer. Derimod er der intet særligt sammenhæng mellem de corticale fund og EEG. Et abnormt EEG under 1 års alderen er et dårligt tegn, hvorimod et normalt EEG i denne aldersklasse ikke tillader den modsatte slutning. 3. ventriklerne med svær dilatation er oftest forbundet med abnormt EEG, men ikke af nogen speciel type.

Kapitel V: Her omtales 63 patienter, på hvem der er foretaget mere end et PEG. Dette må anses for et væsentligt bidrag til vurdering af pålideligheden af fundene og anvendeligheden af ratioer. Det viser sig, at der er særdeles god overensstemmelse mellem de forskellige fund. Hvis undersøgelserne er foretaget med korte mellemrum, er der så godt som ingen forskel i de opnåede ratioer. Er der gået mange år, viser ratio sig ofte konstant, trods store ændringer i kraniediametrene. I en række tilfælde viser det sig, at ratio er tiltaget med årene, og at dette følger med en forværrelse af den kliniske tilstand. Der er ingen patienter, hvor en forværrelse af tilstanden er ledsaget af en formindskelse af dilatationen. Også PEG foretaget på andre afdelinger viser god overensstemmelse, og dette anses som udtryk for, at ved benyttelse af et forholdstal undgår man afhængighed af afstande til røntgenapparater og andre tekniske betingelser, der ville være påkrævede, hvis man anførte de absolutte talværdier.

Kapitel VI: Her omtales ganske kort de foretagne operationer og deres resultater. Der har været god effekt i tilfælde, hvor det har drejet sig om fjernelse af meningo-cerebrale cicatricer. Congenitte misdannelser af forskellig art og sværere perinatale skader har ikke vist de samme gunstige resultater, dog er der patienter, hos hvem der er fjernet cyster, hvor tilstanden er bedret meget.

Kapitel VII: De patologisk-anatomiske fund gennemgås. Cortexbiopsierne, der skønt små og ofte ikke tilstrækkelige til, at der kan afgives noget endeligt svar, har ikke i noget tilfælde være misvisende ved at rejse mistanke om en alvorlig lidelse, der ikke siden er bekræftet. Operationspræparaterne kan bekræfte de fund, der er iagttaget ved indgrebene, men siger ikke meget om ventrikelsystemet.

Materialet af døde patienter gennemgås, og det vises, at dødsårsagerne oftest er febrile lidelser, enten pneumoni eller bronchitis eller i en række tilfælde uopklarede, eventuelt cerebrale hyperpyrexier. I denne forbindelse gøres der opmærksom på mulighed for angstreaktioner og dermed udløst »Voodoo« dødt.

Af de 58 døde er der foretaget sektioner på 22 patienter, og disse gennemgås detaljeret. Det viser sig her, som ved de gentagne PEG, at insufflationerne har vist forandringer, der kan genfindes, og kun i et enkelt tilfælde har der været mulighed for misvisende oplysning baseret på den corticale luft, der dog ikke var stationær, men skiftede side ved 2 undersøgelser.

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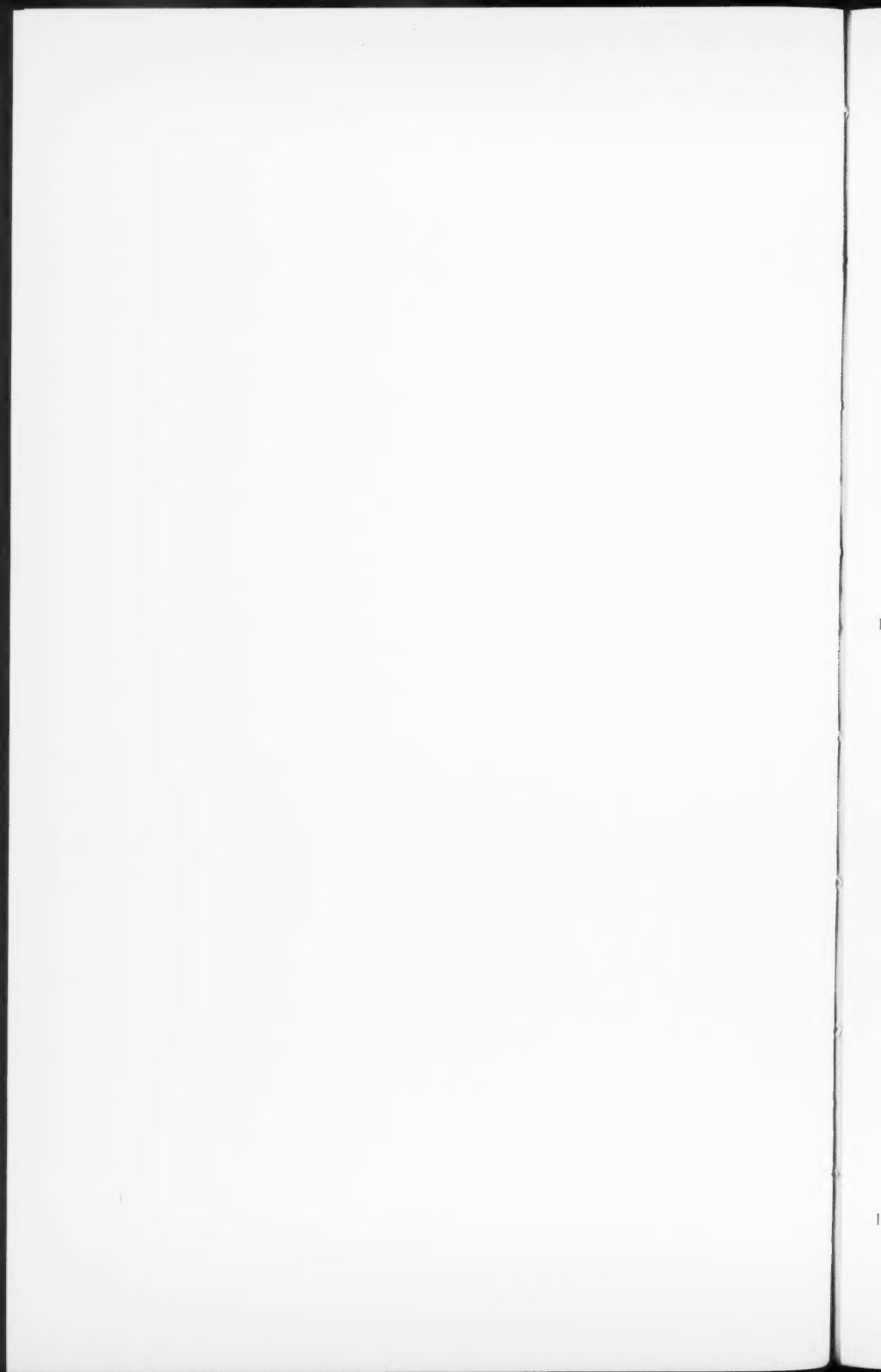
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ILLUSTRATIONS
of different P.E.G. findings and of
autopsy material

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III



Fig. 6 (case no. 2).

11 year old girl. Postnatal aetiology. Removal of meningo-cerebral scar. V.E.G: bilateral dilatation with equal ratios and no displacement. Ratio 0.27. Healthy at follow-up.



Fig. 7 (case no. 27).

1 year 3 mth. old boy. Presumably postnatal aetiology. V.E.G: bilateral ventricular dilatation with equal ratios and no displacement. Ratio 0.31. Healthy at follow-up.



Fig. 8 (case no. 89).

Boy approximately 4 years old. Aetiology unknown. V.E.G: bilateral dilatation with equal ratios and no displacement. Ratio 0.35. Increased cortical air bilaterally. Died at 4 years 3 mths.



Fig. 9 (case no. 151).

Boy approximately 3 years old. Aetiology: possible congenital toxoplasmosis. V.E.G: bilateral dilatation with equal ratios and no displacement. Ratio 0.80. Under institutional care.



Fig. 10 (case no. 154).

5 mth. old boy. Postnatal aetiology. V.E.G: bilateral dilatation with equal ratios. Ventricular system displaced 5 mm. to left. Ratio 0.30. Air collection corresponding to right Sylvian fissure. At follow-up dysarthria, slight right-sided hemiplegia and mental retardation.



Fig. 11 (case no. 176).

Boy approximately 3 years old. Aetiology unknown. V.E.G: bilateral dilatation with equal ratios and displacement of the ventricular system 9 mm. to left. Ratio 0.37. Surface air normal. Follow-up: in a mental institution (idiotia) with severe defect of vision.

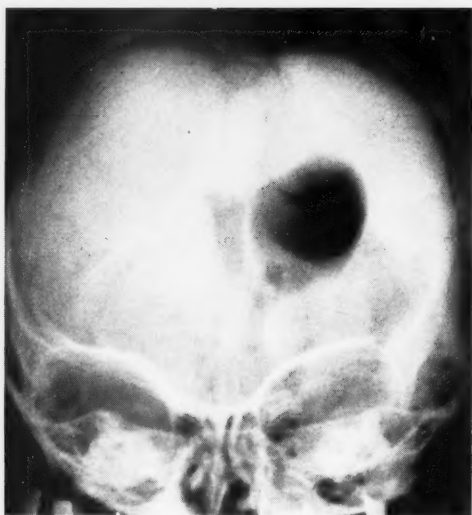


Fig. 12 (case no. 196).

1 year 6 mth. old boy. Aetiology asphyxia. S.E.G: unilateral dilatation. Ratio 0.34 (0.19/0.50). Displacement of the ventricular system 6 mm. to left. Follow-up: right-sided spastic hemiplegia, otherwise healthy.



Fig. 13 (case no. 200).

1 mth. old boy. Aetiology: gastro-intestinal infection with *B. coli*. S.E.G: bilateral ventricular dilatation with unequal ratios. Ratio 0.29 (0.25/0.32). Increased surface air on right side, especially corresponding to the Sylvian fissure and insula. Healthy at follow-up.

VII

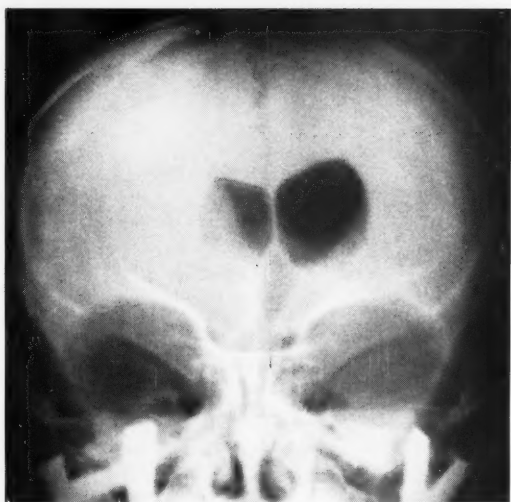


Fig. 14 (case no. 245).

1 year 6 mth. old boy. Aetiology: postnatal. S.E.G: bilateral dilatation with unequal ratios and displacement of the ventricular system 10 mm. to left. Ratio 0.34 (0.29/0.41). Follow-up: right-sided spastic hemiplegia, epilepsy and possible sub-normal intelligence.

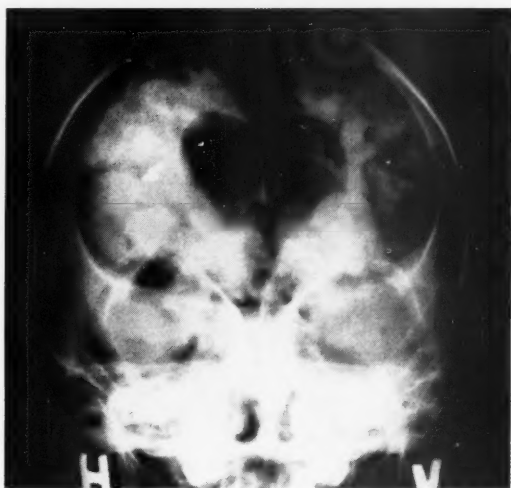


Fig. 15 (case no. 256).

7 mth. old boy. Aetiology: perinatal. V.E.G: bilateral dilatation with unequal ratios and displacement of the system. Ratio 0.40 (0.37/0.44). Greatly increased cortical air bilaterally. Follow-up: died at 14 mth.

VIII



Fig. 16 (case no. 269).

5 year old boy. Aetiology: Rhesus incompatibility. V.E.G: bilateral dilatation most pronounced on the right side. System displaced to the left. Ratio 0.60 (0.64/0.51). A cyst occupying the frontal lobe was removed. Follow-up: post-operatively healthy. Left-sided hemiplegia. Normal intelligence and no seizures.

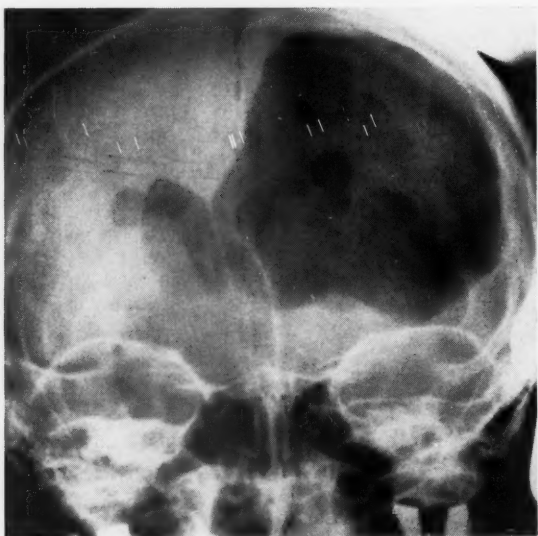


Fig. 17 (case no. 270).

13 year old boy. Aetiology: family predisposition and prenatal factors. V.E.G: pronounced dilatation of the left side and displacement of the ventricular system 25 mm. to the right side. Ratio 0.65 (0.31/0.89). Follow-up: right-sided spastic hemiplegia. Normal intelligence and full working capacity.

IX



Fig. 18 (case no. 84).

6 mth. old boy. Aetiology: pre- and perinatal. S.E.G: bilateral symmetrical dilatation. Over the left hemisphere there is collection of air which communicates with the ventricular system. The septum pellucidum is absent. The defect was opened at operation and found to be a cyst. Follow-up: imbecililas, spastic tetraplegia.



Fig. 19 (case no. 101).

2 mth. old boy. Aetiology: family predisposition, asphyxia for 20 minutes. V.E.G: equal bilateral dilatation with no displacement. Ratio 0.36. Large multilocular porencephaly on the right side. Follow-up: in a mental institution, idiotia.



Fig. 20 (case no. 110).

14 year old boy. Aetiology: family predisposition and postnatal. V.E.G: bilateral dilatation with equal ratios and no displacement. Ratio 0.37. A communicating cyst of the septum pellucidum can be seen. Died at 18 years of age.



Fig. 21 (case no. 64).

10 year old boy. Aetiology: family predisposition. V.E.G: bilateral dilatation with equal ratios and no displacement. Ratio 0.34. There is increased distance between the lateral ventricles such as seen in cases of non-communicating septum cysts. This was supported at a later examination by the fact that the cyst had disappeared. Follow-up: under epileptic care. Retarded.

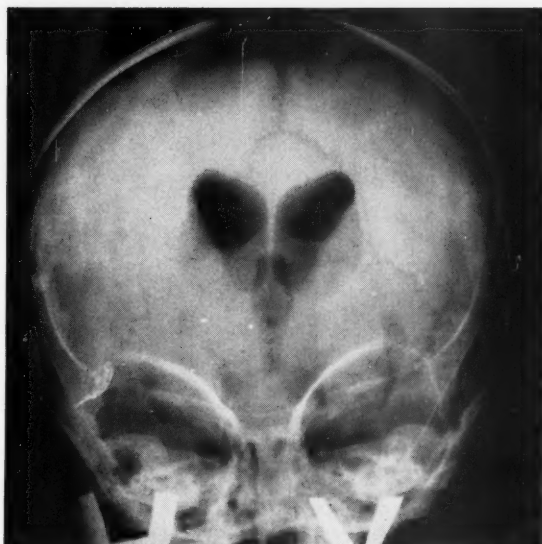


Fig. 22 (case no. 121).

1 year 4 mth. old boy. Aetiology: prenatal complications, prematurity and neonatal gastroenteritis. S.E.G: bilateral dilatation. Ratio 0.39. Enlarged third ventricle: 11 mm. The child died within 24 hours of examination which was supplemented by burr holes. These revealed increased fluid and thickened arachnoid.

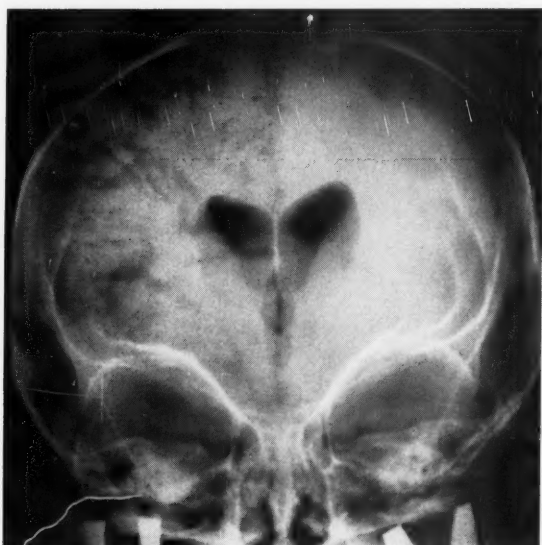


Fig. 23 (case no. 43).

2 year old girl. Aetiology: difficult delivery. S.E.G: bilateral dilatation. Ratio 0.32. Enlarged third ventricle: 10 mm. Normal surface air on the right side. Died within 24 hours of the examination with hyperpyrexia and brain stem convulsions.

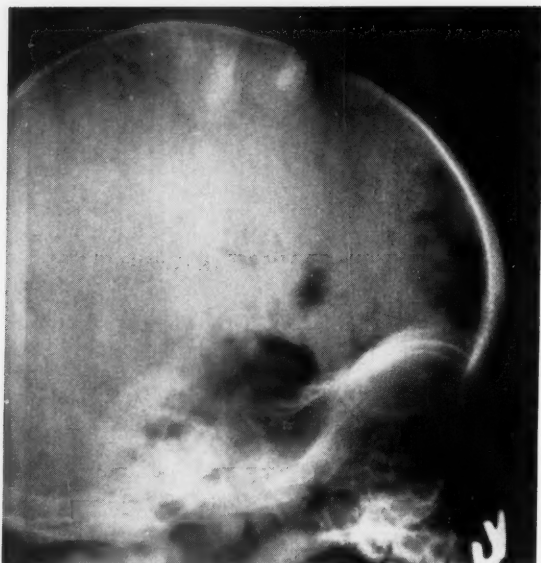


Fig. 25 (case no. 83).

6 mth. old boy. Aetiology: perinatal. V.E.G: first attempt showed no filling of the ventricular system. Air was shown on the surface frontally.

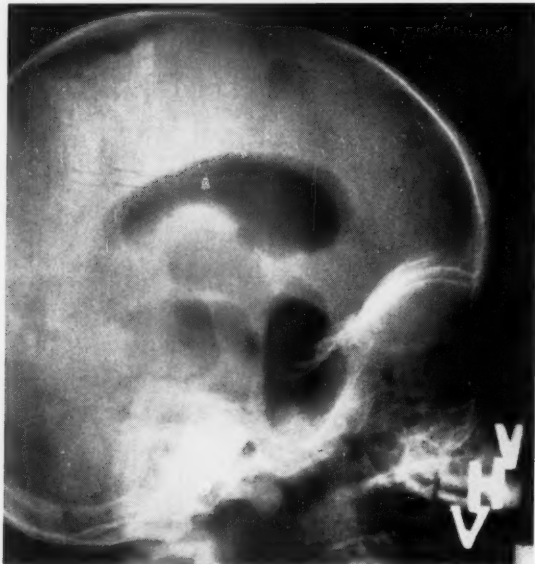


Fig. 26 (same patient).

Second V.E.G. performed a few days after the above examination. System is filled and there is no frontal air collection.

XIII

Figs. 37, 38, 39 (case no. 213).

Girl. Aetiology postnatal.

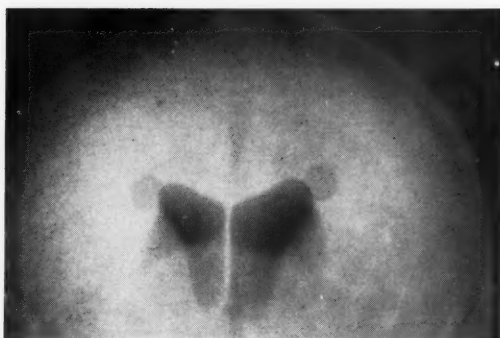


Fig. 37.

7 years old. V.E.G: bilateral dilatation with unequal ratios. No displacement. Ratio 0.36 (0.33/0.39).



Fig. 38.

11 years old. S.E.G: ratio 0.39 (0.34/0.44).



Fig. 39.

11 years old. V.E.G: increased dilatation on left side. Ratio 0.56 (0.44/0.68). Operation performed on left side with removal of atrophic tissue. At follow-up there had been no progression of the disease. Diagnosis: right spastic hemiplegia, epilepsy and intellectual inferiority.

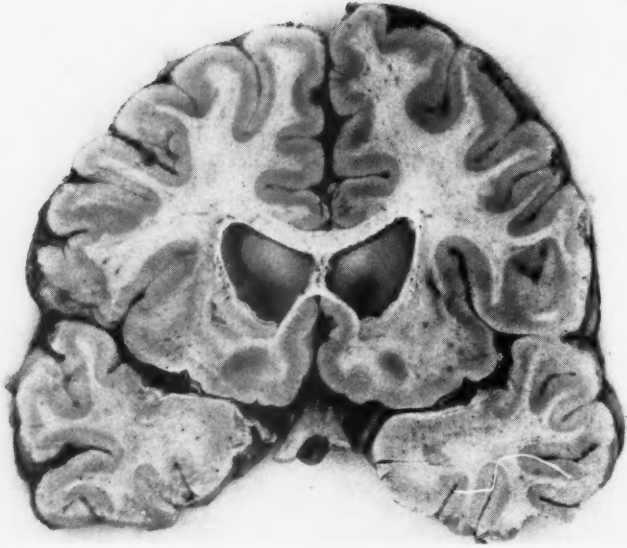


Fig. 40 (case no. 96).

10 year old boy. Frontal section of the brain showed the ventricular system to be moderately dilated corresponding to the ratio found, 0.37. Destruction of the caudate nucleus is seen changing the contour of the outer wall of the lateral ventricle from convex to concave.

6
m

A
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B

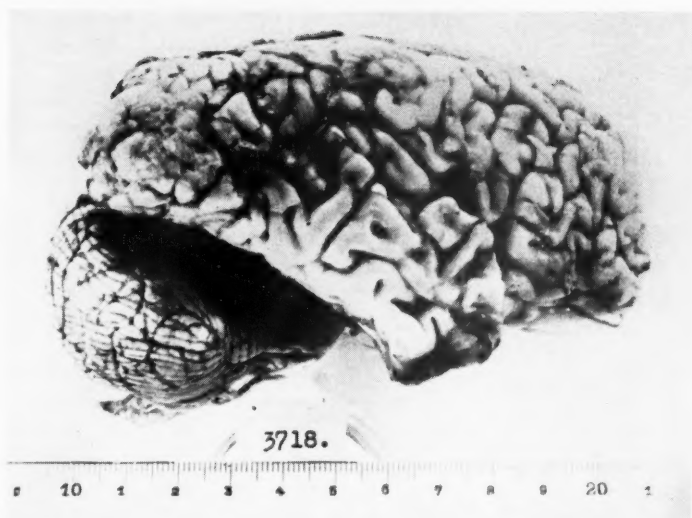


Fig. 41 (case no. 112).

6 year old girl. Microgyri can be seen especially in the frontal and occipital areas. Furthermore it can be seen that the cerebellum is relatively large compared with the cerebrum.

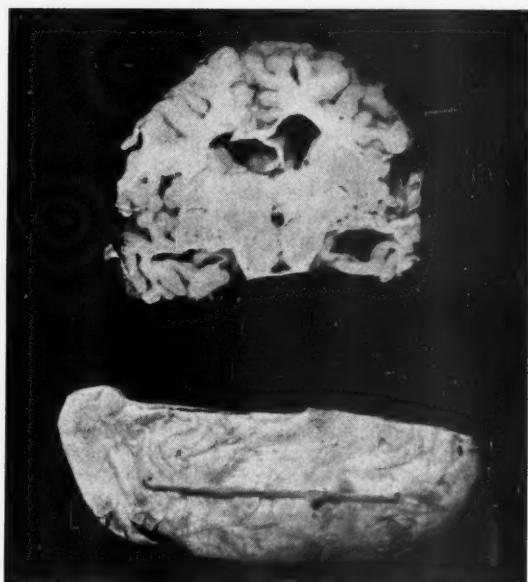


Fig. 42 (same patient).

A: Above: frontal section of the brain showing moderate dilatation of the ventricular system.

Ratio 0.37.

B: Below: membranes consisting of the thickened dura.

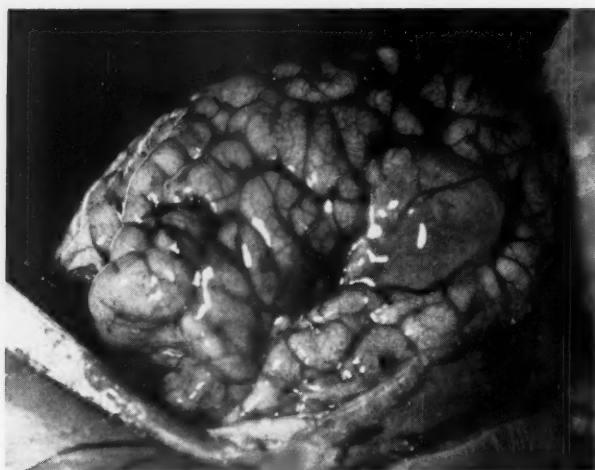


Fig. 43 (case no. 217).

2 year old boy. Large cyst can be seen on the left side corresponding to the Sylvian fissure. The cyst leaked on removal but in the picture can be seen refilled with water.

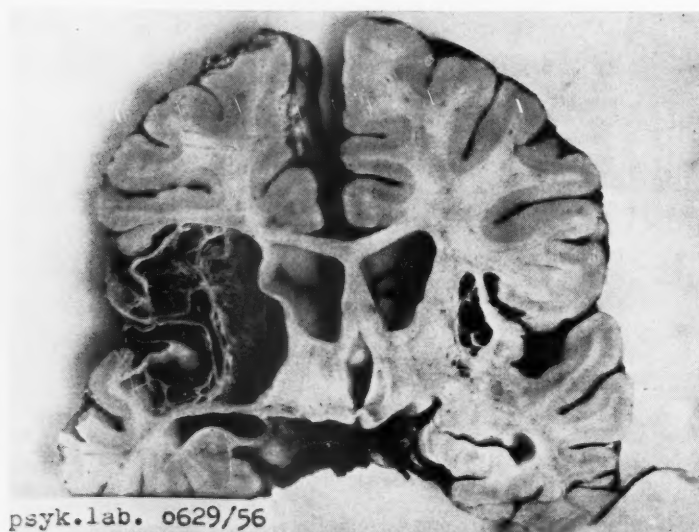


Fig. 44 (same patient).

Brain seen on frontal section. Cystic area corresponds to cyst on surface and does not communicate with the ventricular system. Degree of dilatation corresponds to the ratio shown 0.34/0.44.



Fig. 45 (case no. 268).

2 year old girl. Pronounced microgyri were found in both hemispheres and the cerebrum appeared small compared with the cerebellum.

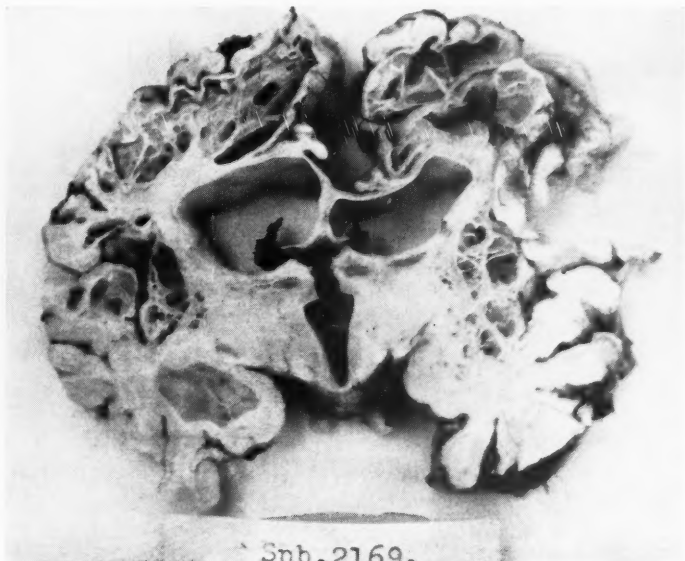
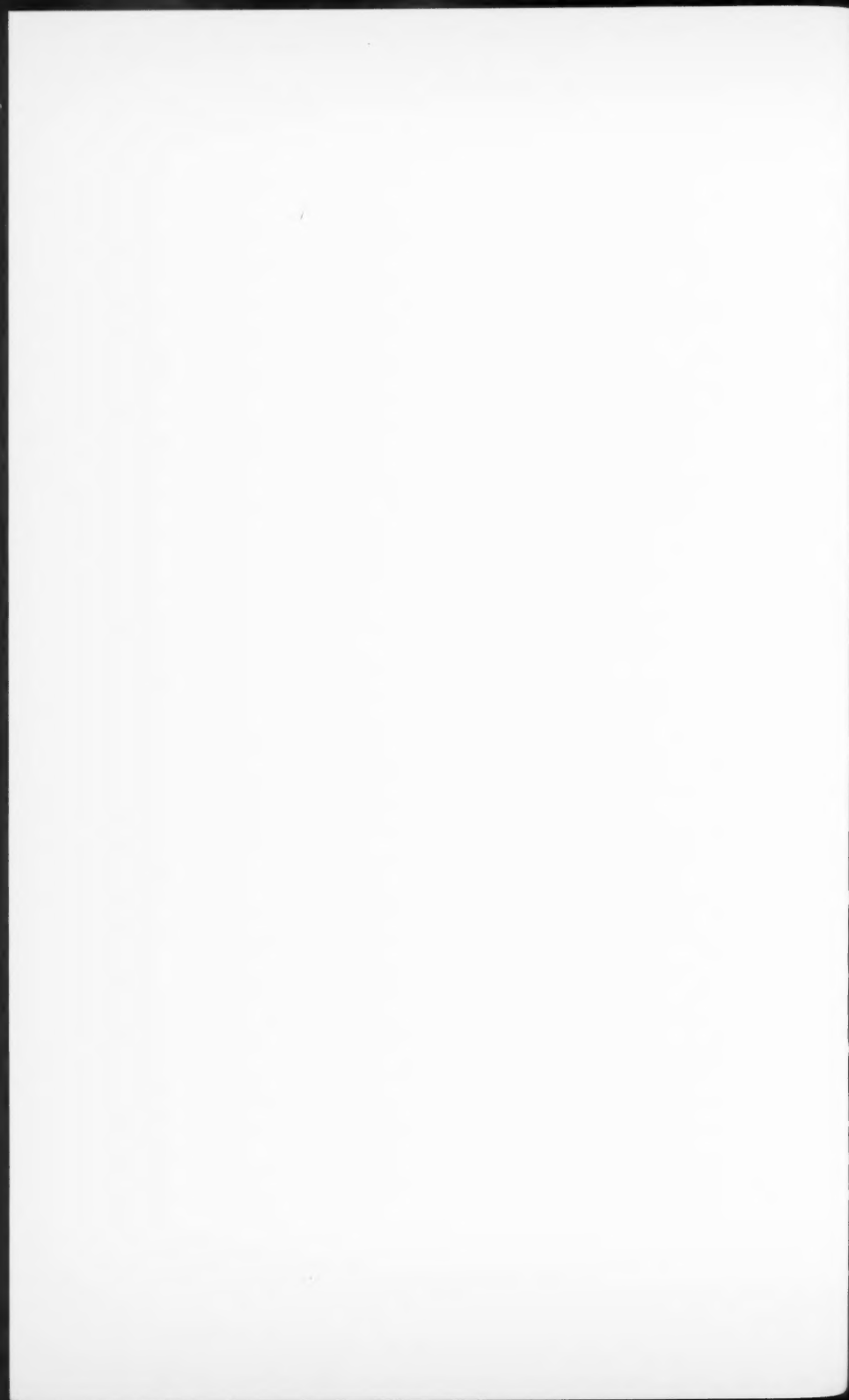


Fig. 46 (same patient).

On frontal section pronounced polyporencephaly was found. Ventricular system severely dilated. Ratio at an earlier time 0.46/0.66.



CASE HISTORIES

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Key to case history numbers in relation to type of P.E.G. and ratio.

	Bilateral ventricular dilatation with equal ratios on both sides		Unilateral ventricular dilatation	Bilateral ventricular dilatation with different ratios on both sides	
	without displacement	with displacement		without displacement	with displacement
≤ 0.29	1- 21		184-195	198-200	232
0.30-0.34	22- 84	153-169	196	201-210	233-246
0.35-0.39	85-125	170-177	197	211-218	247-252
0.40-0.49	126-142	178-180		219-228	253-261
≥ 0.50	143-152	181-183		229-231	262-271

Key to abbreviations used in the case histories

P.E.G. = pneumoencephalography, any form of intracranial air.

V.E.G. = ventriculography.

S.E.G. = sub-occipital encephalography.

L.E.G. = lumbar encephalography.

R.H. = Rigshospital.

N.K. no. = case record no. from the Neurosurgical Department, Rigshospital.

N.K. department = Neurosurgical Department, Rigshospital.

1.

N.K. no. 4007/43. Boy born 18.4.31. No familial predisposition. Pregnancy and delivery normal. Birth weight unknown.

Symptoms: 5 months prior to admission sustained a head injury at school when he was pushed over and hit the back of his head. He was dizzy and had a headache but did not lose consciousness. He was kept in bed for a week. Over the next five months he suffered from intermittent pressure-type parieto-occipital headache which was aggravated by bending and coughing. Was very tired at that time.

Admitted to N.K. department at the age of 11 years 10 months. Tender over the back of the head and to the right. Normal, healthy appearance. Eye examination and all other neurological examinations normal. Skull X-ray: large venous grooves. E.E.G. not done.

V.E.G.: normal pressure. Ratio 0.26 (0.26/0.26). 3rd ventricle 5 mm. Temperature 38.2° C. the same day, otherwise no complications.

Follow-up: since the accident his headache has begun at 10 a.m. and intensified over the next 2-3 hours. It is aggravated by physical exertion. In recent years it has become less frequent and he may go for several months without it. He is a medical student and able to carry out his duties without difficulty. He studies without discomfort. He had a nervous breakdown accompanied by increased headache at the age of 18 while studying for his examinations. Admitted to hospital for two months. No special investigations carried out. Physical examination: completely normal and healthy appearance. Mental and physical state normal. Reflexes normal.

Diagnosis: headache (decreasing), healthy.

Summary: a boy who at about 11½ sustained a head injury followed by headaches. V.E.G. when almost 12 years old showed a ratio of 0.26, 3rd ventricle 5 mm. Has done well since. Had increased headache and a nervous breakdown during medical studies but is otherwise healthy.

2.

N.K. no. 7797/46. Girl born 13.5.34. No relevant family history. First of three children. Pregnancy and delivery normal. Birth weight 3125 g.

Symptoms: involved in a road accident at the age of 5 years and sustained a fractured skull. Unconscious for 24 hours. Bone fragment removed from right temporal region and she remained in hospital for two months. Was then symptom-free until a year before admission when seizures of 2-3 seconds' duration began to occur up to six times a day. School progress was good.

Admitted to N.K. department at the age of 11 years 10 months. Scar measuring 1×2 cm. placed vertically above the right ear with an underlying bone defect and visible and palpable pulsation. Neurological examination normal. Psychological state normal. X-ray of skull revealed a defect in the right parietal region and rather coarse basal markings. E.E.G. showed typical epileptic formations.

V.E.G.: pressure 80, clear fluid. Ratio 0.27 (0.29/0.25). 3rd ventricle 3 mm. Incision made over the defect and a 2 cm. long typical meningo-cerebral scar revealed. No post-operative complications apart from slight fever. Microscopy showed a meningo-cerebral scar with early angioma formation.

Follow-up: admitted to a hospital for epileptics for a month at the age of 14 years. Diagnosis: possible epilepsy. At that time she was doing well at school and there was no neurological abnormality. E.E.G. showed fairly severe dysrhythmia. Right-sided arteriography showed a vessel-free area corresponding to the site of operation. L.E.G. ratio 0.27 (0.29/0.26). 3rd ventricle 5 mm. Right side - 7 mm. Patient has been completely well since. She has some headache localised to the operation area. Is married, has two

children and both deliveries were uncomplicated. No eye trouble. Physical examination: fit and well. A defect can be felt in the right parietal region. No pulsation over the area. No neurological abnormality. Head circumference 53 cm.

Diagnosis: possible petit mal, otherwise healthy.

Summary: a girl who sustained a fractured skull at the age of 5 years. No symptoms until almost 11 years old when she developed short-lasting seizures. V.E.G. at 11 years 10 months showed a ratio of 0.27, 3rd ventricle 3 mm. Operation for removal of meningo-cerebral scar performed. Has been completely well since the age of 14 years.

3.

N.K. no. 8505/46. Boy born 5. 7. 36. No familial predisposition. Second of three children. Normal pregnancy and delivery. Birth weight 4500 g.

Symptoms: hit on the left side of the head when 3 years old. There was bruising but no complications. Four years before admission had generalised epileptic seizures accompanied by tonic and clonic spasms and loss of consciousness. Attacks usually occurred during the evening and were followed by pain. Two years elapsed between the first and second attacks and thereafter they occurred about once a year. During the year prior to admission there were five convulsions followed by short-lasting weakness. Admitted to R.H. Neuromedical Department at the age of 8 years L.E.G. showed the left lateral ventricle to be slightly more dilated than the right. Admitted to a hospital for epileptics at the age of 10 years. Second L.E.G. showed filling on the left side only. Ratio 0.30. E.E.G.: severe dysrhythmia. Eyes normal.

Admitted to N.K. department at the age of 10 years. Eye and neurological examination normal. Healthy child. E.E.G. and skull X-ray not done.

V.E.G.: pressure 180. Ratio 0.27 (0.25/0.29). 3rd ventricle 3 mm. Temperature 37.8° C. on the day of examination and some headache. Otherwise no complications.

Follow-up: no seizures since the age of 12 years. Left school at normal age and successfully learnt a trade. Physical examination: healthy, normal appearance. Neurological and eye examination normal. Mental state and speech normal. Head circumference 58 cm. Rejected for Army service.

Diagnosis: healthy.

Summary: a boy who at 3 years of age had a head injury followed 3 years later by generalised convulsions. V.E.G. at 10 years showed a ratio of 0.27, 3rd ventricle 3 mm. Has been seizure-free from the age of 12 and is completely healthy.

4.

N.K. no. 9356/47. Boy born 6. 12. 38. No familial predisposition. Second of five children. Normal pregnancy and delivery. Birth weight 3775 g.

Symptoms: hit by a stone on the left side of the head at the age of 6 years. Two and a half years before admission complained of headache on running and similar physical exertion. Eighteen months before admission episodes of falling after running accompanied by severe headache. Appeared to lose his balance and he himself felt dizzy. Attacks ceased after running and similar exercise had been banned for a year.

Admitted to N.K. department at the age of 8 years 10 months. Eye examination normal. Tendon reflexes brisk. No Babinski. Skull X-ray showed nothing abnormal apart from thin walls. E.E.G. not done.

S.E.G.: pressure 200. Clear fluid. Ratio 0.27 (0.24/0.29). 3rd ventricle 6 mm. Temperature 38.9° C. the day after the examination. No other complications.

Follow-up: no headache since last admission. Patient has worked for some years on a farm and is doing well. He is a particularly good footballer. Physical examination: eye and neurological examination normal. Head circumference 57.5 cm. Speech normal and no psychological abnormality present.

Diagnosis: healthy.

Summary: a boy who had a head injury at the age of 6 years followed 2½ years later by headache and episodes of falling. S.E.G. at 8 years 10 months showed a ratio of 0.27, 3rd ventricle 6 mm. At follow-up was completely healthy.

5.

N.K. no. 05665 b/50. Boy born 24. 10. 36. No familial predisposition. Third of six children. Normal pregnancy and delivery. Birth weight 3500-4000 g.

Symptoms: 15 days prior to admission sustained concussion after falling from barn roof. No loss of consciousness but he vomited and had a headache. Admitted to hospital for a week because of a fracture of the left clavicle and haematoma round the right eye. Was confused and talked nonsense. Left pupil seen to be larger than right. Two days later his temperature rose to 40° C. and he vomited. A depressed fracture 10 mm. in diameter could be felt. Operation performed. An L-shaped depression fracture involving the forehead and the orbit was found. The dura was intact. Small blood clots were removed and incision closed. Three days after operation there was increased discharge from the left nostril which lasted a few days.

Admission to N.K. department at the age of 13 years 5 months. Scar present on the right side of the forehead. Eye examination: fractured orbit. Left pupil larger than right. No rhinorrhoea. Patient discharged.

Second admission to N.K. department at 13 years 6 months. Had been well until beginning of the month when sight of left eye decreased. 12 hours later he developed headache, fever, malaise and vomiting. Admitted to hospital where marked neck stiffness was found. Lumbar puncture showed a pressure of 500 and 1600/3 cells. Treated as a case of purulent meningitis and made a good recovery. On that admission eye examination showed incipient atrophy of left optic nerve. Further otological and neurological examination normal. E.E.G. not done.

S.E.G.: pressure 110, clear fluid. Ratio 0.27 (0.29/0.25). 3rd ventricle 4 mm. Temperature 38.4° C., normal next day. Discharged to another hospital.

Third admission to N.K. department at the age of 13 years 7 months. Had been well until the middle of the month when he again developed symptoms of meningitis and was re-admitted to hospital. Had malaise and pains in his neck, vomited and had a temperature of over 40° C. 20/5 protrusion of right eye and pain on pressure around it. Lumbar puncture: pressure 500, numerous cells. On that admission the left-sided optic nerve atrophy was found to be more pronounced than previously. Skull X-ray showed depression of right supra-orbital margin.

Operation medial to the frontal sinus revealed a $2 \times 2\frac{1}{2}$ cm. area of severe inflammation similar to that seen in underlying osteitis. The affected area was removed. On opening the dura the cerebrum was seen to be fixed to the right lamina cribosa. The tissue here was fibrosed and a deep yellow in colour. Electrocoagulation of the right lamina cribosa performed. Bone microscopy showed no abnormality. Post-operatively his temperature rose to a maximum of 39° C. on the fourth day. Otherwise no complications.

Follow-up: the patient is completely well and for the past five years has been farming. No headache or eye symptoms. Speech and mental state normal. Head circumference 55 cm. Scars of operations present. Otherwise no abnormality.

Diagnosis: healthy.

Summary: a boy who at 13 years had a skull fracture and accompanying rise in temperature. S.E.G. at 13½ showed a ratio of 0.27, 3rd ventricle 4 mm. Two months later operation over the frontal sinus revealed an inflamed area which was removed. The patient has since been completely well.

6.

N. K. no. 20456/53. Boy born 25. 8. 52. No familial predisposition. Only child. Pregnancy normal. Delivery somewhat prolonged but normal otherwise. Birth weight 2850 g.

Symptoms: daily generalised clonic convulsions lasting about 15 minutes from the age of 3 months. Development otherwise normal. Admitted to the R.H. Paediatric Department at the age of 5 months. E. E. G. during a seizure-free period was normal, but during a seizure it was severely abnormal. Sub-dural puncture showed clear fluid. Eye examination normal.

Admitted to N.K. department at the age of 6 months. Eye examination normal. Head circumference 46 cm. Fontanelles bulging. All four limbs moved equally. Reflexes normal.

Seemed a little retarded. X-ray of skull: walls somewhat thin. E.E.G: severely abnormal with large spikes in the right temporal region during attack.

S.E.G: pressure 300, clear fluid. Ratio 0.27 (0.28/0.26). 3rd ventricle 7 mm. Temperature 38.2° C. the day following examination, otherwise no complications.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department and making progress. Is beginning to walk with some support and can sit alone. Still appears to be severely retarded, however, and grinds his teeth. E.E.G. severely abnormal but patient has been seizure-free for several years. Occasionally falls. Enjoys other children's company.

Diagnosis: oligophrenia (imbecility), epilepsy.

Summary: a boy whose delivery was protracted. From the age of 3 months he had generalised convulsions. S. E. G. at 6 months showed a ratio of 0.27, 3rd ventricle 7 mm. Is making progress but is still severely retarded. Has had no seizures for several years.

7.

N.K. no. 22035/54. Girl born 29. 3. 54. No familial predisposition. Last of sixteen children. Mother died half an hour after giving birth, apparently from liver disease. Child was markedly cyanosed and dyspnoeic. There was fairly severe asphyxia at birth. Birth weight 3400 g.

Symptoms: admitted to hospital for the first six weeks of life. At the age of a month had two cyanotic episodes accompanied by contractions of the right leg and left arm. Ceased after administration of oxygen.

Admitted to N.K. department at the age of 6 weeks. Eye examination: neonatal haemorrhagic retinopathy. Tendon reflexes brisk. Bilateral Babinski. X-ray of skull normal. E.E.G. not done. Sub-dural puncture showed clear fluid.

S.E.G: ratio 0.27 (0.29/0.26). 3rd ventricle 2 mm. Surface air within normal limits. No complications after the examination.

Follow-up: has been well since discharge. No seizures. Sat alone at 10 months and walked alone at two years. Speech is excellent. At the age of two is almost toilet trained. Physical examination: head circumference 49 cm. Eye examination normal. Reflexes and motor system normal. Speech and comprehension advanced for age.

Diagnosis: healthy.

Summary: a girl whose mother died half an hour after delivery. Patient was asphyxiated and had convulsions at one month. S.E.G. at 6 weeks showed a ratio of 0.27, 3rd ventricle 2 mm. Is now completely well.

8.

N.K. no. 24116 b/55. Boy born 11. 5. 54. No familial predisposition. Second of two children. Pregnancy complicated by hypertension. Delivery easy and normal. Birth weight 3225 g.

Symptoms: two days after birth he had a cyanotic attack lasting 3-5 minutes. There were no convulsions. Admitted at 5 weeks because of fever and vomiting. Re-admitted for same condition at 3 months. Admitted to R.H. Paediatric Department at 4 months. Did not smile and sight was uncertain. X-ray of skull showed patchy calcification corresponding to ventricles. E.E.G. severely abnormal with total loss of activity. Toxoplasmosis reaction negative.

First admitted to N.K. department at the age of 5 months.

S.E.G: pressure 150. System dilated with porencephaly frontally. Ratio 0.27 (0.27/0.26). 3rd ventricle 6 mm. Calcification as described.

Transferred from the N.K. department to the R.H. Paediatric Department. Out-patient follow-up four months later showed the patient to be increasingly stiff and having further convulsions.

Second admission to N.K. department at 9 months. Burr hole on right side revealed a thick, grey membrane and xanthochrome fluid was removed. Following insufflation narrowed air cavities were seen. Calcification was presumably in the inner haematome membrane.

Operation on the right side showed a 1 mm. thick membrane which was pale and fibrotic.

Operation on the left side two weeks later and removal of 60 ml. fluid. Membrane found to be similar to that seen on the right side. Microscopy showed membrane resembling that of a haematoma several months old with a solitary area of calcification. Following operation temperature was 39.2°C . He remained febrile for several days without alteration in his general condition. Followed up as an out-patient in the R.H. Paediatric Department. Jerks and marked generalised hypertonia present. Re-admitted to R.H. Paediatric Department at the age of 18 months after an episode of vomiting.

Third admission to N.K. department at 19 months.

V.E.G. through previous burr holes. Pressure 275. Xanthochrome fluid present. As anticipated, there were large hygromas on both sides. Considerable atrophy of right hemisphere. Temperature 38.2°C . the day after examination, otherwise no complications.

Follow-up: seen as an out-patient in the R.H. Paediatric Department. Referred to State mental care at the age of 20 months. Repeated E.E.G. examinations showed severely depressed activity. Admitted to a hospital for epileptics at the age of 2 years 5 months and died five days later. According to the hospital notes, his respirations became shallow and quick. Rales could be heard and treatment with penicillin was started. His temperature rose rapidly to 41.5°C . and neck stiffness developed. No autopsy was carried out.

Diagnosis: spastic tetraplegia, oligophrenia (idiotcy?), epilepsy.

Summary: a boy whose mother's pregnancy was complicated by hypertension. He had cyanotic attacks two days after birth. S.E.G. at 5 months showed a ratio of 0.27, 3rd ventricle 6 mm. Operated on for sub-dural haematoma. Died at 2 years 5 months in a hospital for epileptics. Had been severely spastic and mentally retarded.

9.

N.K. no. 9923/47. Boy born 18.9.36. No information on familial predisposition. Only child. Mother vomited throughout pregnancy. Delivery was prolonged and lasted 20 hours. Child was asphyxiated. Birth weight 3300 g.

Symptoms: otitis media when 14 months old with radical operation on the left side. Discharging ear at 5 years. Head injury when riding a bicycle at 7 years. No loss of consciousness. The following day he vomited and had a headache and was in bed for 3 weeks after this. Since then frequent headaches accompanied by vomiting and dizziness, and always following physical activity. Patient had to lie down for 5-6 hours. Over the 12 months prior to admission there had been difficulty in concentration and a poor memory.

Admitted to the department at the age of 10 years 8 months. Eye and neurological examination normal. X-ray of skull showed rather coarse markings with some gaping of sutures. E.E.G. showed moderately severe dysrhythmia.

S.E.G.: pressure 200. Ratio 0.28 (0.28/0.28). 3rd ventricle 2 mm. Temperature 37.8°C . the same day. No abnormality otherwise.

Follow-up: headaches have almost disappeared. Recently found to have bilaterally decreased hearing for very high and very low tones. Has had two episodes of concussion without any apparent ill-effect. Is doing well as a music student. Physical examination: head circumference 56 cm. Eye examination and neurological examination normal.

Diagnosis: slight headache, healthy.

Summary: a boy whose delivery was prolonged and who was asphyxiated. At the age of 14 months he had an ear infection and at 7 years a head injury followed by headaches. S.E.G. at 10 years 8 months showed a ratio of 0.28, 3rd ventricle 2 mm. Has infrequent headaches and some loss of hearing. Is otherwise healthy.

10.

N.K. no. 05572/50. Boy born 14.12.35. No familial predisposition. Fourth of four children. Pregnancy and delivery normal. Birth weight approximately 3500 g.

Symptoms: at 12 years of age sustained injury to left side of head with no loss of consciousness. Headache and dizziness a few hours after the injury. Was in bed for

10 days. Since then has had headache, dizziness, difficulty with recall and emotional instability.

Admitted to N.K. department when 14½ years old. Eye examination: slight astigmatism. Hearing reduced on right side. Skull X-ray: increased venous grooves, otherwise normal.

S.E.G.: pressure 180. Fluid clear. Ratio 0.28 (0.27/0.29). 3rd ventricle 3 mm. Surface air normal. Temperature 38.2° C. the same day, otherwise no complications.

Follow-up: has finished at grammar school and is studying engineering. At 20 years of age had a virus infection with dizziness and collapse. Since examined by different specialists and treated with physiotherapy and chiropractic with only short-lived effect. Had two fainting attacks at that time but no real convulsions. At present is studying and doing well. Physical examination revealed no abnormality. Head circumference 56 cm. Eye examination normal. Neurological examination normal.

Diagnosis: headache. Otherwise healthy.

Summary: boy who sustained head injury at 12 years of age with subsequent headache, dizziness etc. *S.E.G.* performed at 14½ years of age. Ratio 0.28. At follow-up there had been some fainting attacks but for the last few years he had been perfectly well.

11.

N.K. no. 07853/51. Girl born 4. 4. 51. No familial predisposition. Third of three children. Pregnancy normal. Delivery difficult. Had injections. No asphyxiation. Birth weight 3600 g.

Symptoms: since birth tendency to opisthotonus. No neonatal jaundice. Alternately stiff and flaccid with aimless movements of the upper extremities. Admitted to hospital and transferred to the R. H. Paediatric Department where she developed generalised convulsions. Subdural puncture: no fluid but later a little bloodstained exudate from the puncture holes.

Admitted to N.K. department at 4 months of age. Eye examination normal. Follows light. Head circumference 40 cm. Increased motor activity. Reflex examination could not be performed but a tendency to bilateral Babinski was found. E.E.G. showed possible changes in the left hemisphere. Subdural puncture: no fluid.

V.E.G.: pressure 0. Ratio: 0.28 (0.26/0.30). 3rd ventricle 8 mm. Lateral ventricles are widely separated with elevation of 3rd ventricle. (Absence of callosal body?). No surface air. Temperature 38° C. on the day of examination. Otherwise no complications.

Follow-up: admitted to the R. H. Paediatric Department on two occasions and recommended to State mental care. Died in hospital at the age of 15 months from measles, bronchitis and pneumonia.

Diagnosis: oligophrenia.

Summary: girl whose delivery was difficult. Tendency to opisthotonus, alteration of muscle tone and generalised convulsions since birth. *V.E.G.* at 4 months of age showed ratio of 0.28. Possible absence of callosal body. Recommended for State mental care but died at 15 months of age.

12.

N.K. no. 08540/52. Boy born 4. 4. 42. No familial predisposition. Second of three children. (First child died during delivery). Pregnancy normal. Breech presentation and forceps delivery. No asphyxia. Birth weight 3700 g.

Symptoms: when one year of age had otitis media. At 4 years of age had a serious head injury. Was in bed for 8 days. Treated for anorexia at 2 and 7 years of age in a paediatric out-patient department. At 8 years of age admitted for investigation of possible epilepsy. Since 5 years of age had had nightly seizures with muscular contractions around the mouth but no actual convulsions. The seizures lasted for a maximum of ¾ hr. and he went on sleeping. They gradually decreased in frequency. At 8 years of age had seizures during the daytime of approximately 20 minutes' duration and in addition petit mal and contractions around the mouth. Admitted to children's hospital at that age. E.E.G. showed paroxysmal dysrhythmia with a focus in the right temporal region. Admitted to R.H. Neuromedical Department at 9 years of age. L.E.G. showed a lack of filling of the right lateral ventricle. E.E.G. showed moderate dysrhythmia in the right temporal region.

Readmitted to children's hospital at 9½ years of age. After treatment with phenobarbitone had been discontinued there were repeated seizures.

Admitted to N.K. department when 9 years 9 months old. Eye examination and full neurological examination entirely normal. Skull X-ray also normal. E.E.G., as previously, showed spike focus in the right temporal region.

S.E.G.: pressure 180. Clear fluid. Ratio: 0.28 (0.27/0.28). 3rd ventricle 6 mm. Normal distribution of surface air. No temperature or other complications after the examination.

Follow-up: completely normal child. Occasional affect reaction which soon disappears. No seizures during past 4 years. Left school at 14 years of age and has worked since. Physical examination: head circumference 56 cm. Eye examination and neurological examination showed nothing abnormal. Appeared to be psychologically normal.

Diagnosis: healthy.

Summary: boy who had a delivery of long duration with breech presentation. Sustained serious head injury at 4 years of age. Seizures at 5 years of age. *S.E.G.* when 9 years 9 months old showed a ratio of 0.28. At follow-up had had no seizures for the previous 4 years, was working and appeared mentally and physically normal.

13.

N.K. no. 21472/53. Boy born 25. 5. 39. No familial predisposition. Second of six children. Pregnancy normal. Delivery four weeks premature. Birth weight over 2000 g.

Symptoms: complained of headache from the age of 3–4 years. At about 10 years of age sustained a head injury without loss of consciousness, but accompanied by nausea and vomiting. When 12 years old hit his head when skating. On this occasion there was loss of consciousness for a short time with nausea and vomiting. Headache became worse after this and was localised behind the eyes. Had always had tics and been nervous. Normal school progress.

Admitted N. K. department when 14½ years old. Eye examination and neurological examination normal. Appeared to be somewhat immature. X-ray of skull: no abnormality apart from deep posterior fossa. E.E.G: slight to moderate abnormality.

S.E.G.: pressure 200, clear fluid. Ratio 0.28 (0.27/0.29). 3rd ventricle 3 mm. Normal distribution of surface air. Temperature 37.9° C. the same day, otherwise no complaints.

Follow-up: has been entirely well since insufflation. Is training to be a car mechanic and doing well. Physical examination: head circumference 56.2 cm. Normal, healthy appearance. No neurological abnormality. No eye symptoms. Speech and mental state normal. No tics.

Diagnosis: healthy.

Summary: boy with a birth weight a little over 2000 g. Complained of headache from the age of 3 years, exacerbated by head injuries at the age of 10 and 12 years. Loss of consciousness occurred with the last injury. *S.E.G.* at the age of 14½ showed a ratio of 0.28. At follow-up he had been entirely fit since insufflation.

14.

N.K. no. 23145/55. Girl born 26. 12. 48. No familial predisposition. Second of two children. Bled frequently during pregnancy and fainted repeatedly. Haemoglobin at end of pregnancy 52%. Delivery two weeks overdue. Slight asphyxiation. Birth weight 3700 g.

Symptoms: head injury when 5 years 8 months old, possibly accompanied by loss of consciousness. Stayed in bed 24 hours and was very listless. During the following 8 months she had 4 seizures in which she appeared frightened, and her head turned to the left; there was squinting, decrease of vision almost to blindness and contractions of the limbs on the left side. Admitted to the R. H. Paediatric Department at 6 years of age. *L.E.G.*: ratio 0.26 (0.28/0.25). 3rd ventricle? E.E.G: severely abnormal with focus of low frequency over the left hemisphere.

Admitted to N.K. department when 6 years 3 months. Left-handed. Latent convergent squint. Reflexes normal. Skull X-ray normal.

V.E.G.: pressure 100. Only partial filling of the system achieved so that complete assessment could not be made. Left-sided arteriography normal.

S.E.G.: pressure 300. Ratio 0.28 (0.27/0.28). 3rd ventricle 2 mm. No complaints after the examination.

Follow-up: no seizures since discharge. Awoke screaming on a single occasion but had no convulsion. Medicine discontinued. Does well at school and gets on well with other children. Has just had glasses because of long-sightedness. Physical examination: head circumference 52 cm. Eye examination and reflexes normal. Repeated E.E.G. still severely abnormal and for this reason anti-convulsant therapy was re-instituted.

Diagnosis: epilepsy (infrequent seizures). Healthy otherwise.

Summary: girl whose mother bled during pregnancy. Patient was asphyxiated at birth. Sustained head injury at 5 years 8 months with possible loss of consciousness. Seizures followed after this. S.E.G. at 6 years 3 months showed a ratio of 0.28. At follow-up had had only one doubtful seizure but E.E.G. showed continued abnormality. Doing well at school.

15.

N.K. no. 01175a/48. Girl born 9.9.41. Mother's mother has epilepsy. Third of three children. Pregnancy normal. Birth difficult because of the mother's flattened and narrowed pelvis. Child was turned and manually extracted and was severely asphyxiated for about 50 minutes. Birth weight 3100 g.

Symptoms: during the second 24 hours is was noticed that the right-sided limbs were paralysed. This gradually disappeared. When a year old she had an episode of loss of consciousness but without any convulsion. Seizure-free for the next 2 years. During the 3 years prior to admission had a total of 6-7 similar attacks. Admitted to a children's hospital on the last occasion at the age of 6 years 2 months. I.Q. 76. Always rather retarded in development.

Admitted to N.K. department at 6 years 4 months. Eye examination normal. Is left-handed with reduced muscle tone and appeared of slightly reduced intelligence. Reflexes normal. E.E.G.: moderate diffuse dysrhythmia with scattered epilepsy formations on special recordings. X-ray of skull: slightly increased markings, otherwise normal.

S.E.G.: pressure 550, clear fluid. Examination abandoned because of high pressure. After the patient had been unconscious almost the whole day V.E.G. was performed. Pressure 80. Ratio 0.29 (0.28/0.31). Third ventricle impossible to measure. Temperature 38.1° C. the same day, normal two days later. Otherwise no complaints.

Re-admitted one week after discharge for treatment of wound haematoma. The patient had developed neck stiffness but this disappeared.

Follow-up: followed up as an out-patient in the Orthopaedic Hospital's cerebral palsy clinic. *Diagnosis*: cerebral palsy (striato-cerebralis) as a sequelae of neonatal asphyxia. Chorea. Possible intellectual inferiority. Dysarthria. Patient had attended a State Institution for speech difficulties and later a special school. I.Q. in 1954 64. Social evaluation: education cannot be considered because she is below the one-third limit of capability, and she is eligible for chronic sickness help. Had only one seizure shortly after discharge. Manages to look after herself. Attends gymnastic classes and physiotherapy.

Physical examination: head circumference 54 cm. Eyes normal. There are increased patellar responses, no ankle clonus but bilateral Babinski. Tendon reflexes in arms are brisk. Patient has a pattern of movement and position of the athetoid-dystonic type with dysarthria. Intellectually appears much better than the I.Q. of 64 would indicate.

Diagnosis: athetosis (dystonia), right side more than left. Dysarthria. Debilitas mentis with intellectual inferiority.

Summary: girl with maternal familial predisposition to epilepsy. 50 minutes' asphyxia at birth. From the second day of life had paralysis of the right-sided limbs which gradually disappeared. Episode of unconsciousness at one year of age. V.E.G. ratio at 7 years was 0.29.

At follow-up she qualified for chronic sickness help because of cerebral palsy of athetoid-dystonic type with some mental retardation.

16.

N.K. no. 01244/48. Boy born 27.2.44. No known familial predisposition. Second of two children. Pregnancy normal. Birth said to be one month premature, not particularly

difficult. Asphyxia of unknown duration. Birth weight about 3500 g. Slight jaundice was present for the first week.

Symptoms: had always been somewhat weak in right arm and leg. This became really obvious when the patient began to walk. Admitted to R.H. Neuromedical Department.

Admitted to N.K. Department when 4 years old. On physical examination he appeared somewhat retarded in comparison with other children of his age. Eye examination normal. A right-sided hemiparesis was present. X-ray of skull was normal. E.E.G. revealed a number of potentialities of long duration but no definite abnormality.

S.E.G.: pressure 300, clear fluid. Ratio 0.29 (0.29/0.29). 3rd ventricle 4 mm. Normal surface air. No complications following the examination. Burr hole over the left hemisphere in the pre-motor region revealed normal arachnoidea.

Follow-up: followed up as an out-patient in the Orthopaedic Hospital's cerebral palsy clinic for a short time. Is doing very well. Manages school work without difficulty. Can cycle and has tremendous energy. Is particularly clever at arithmetic. Eyes, speech and hearing are all normal. Physical examination: head circumference 56 cm. Eye examination normal. Speech also normal. He makes constant head movements from side to side sometimes accompanied by movements of the shoulders and spine, resembling torsion spasms, and makes athetoid hand and arm movements. Can stand on one leg. Tendon reflexes in arms brisk, presumably pathological. Tendon reflexes in legs: extremely brisk patellar reflexes. No ankle clonus. Doubtful bilateral Babinski.

Diagnosis: athetosis, possibly combined with muscular dystonia (torsion spasms). Normal intelligence.

Summary: boy who was asphyxiated at birth and had slight jaundice for the first week of life. Right arm and leg always weak. S.E.G. at 4 years of age showed a ratio of 0.29. 3rd ventricle 4 mm. At follow-up he had done well at school. He makes constant movements of his head and shoulders resembling torsion spasms and athetosis.

17.

N.K. no. 01601/48. Boy born 16.5.44. No familial predisposition. Pregnancy: placenta praevia. Delivery by Caesarian section, 4 weeks prematurely. Severe asphyxia present. Birth weight 3375 g.

Symptoms: fell and hurt himself many times after he began to walk. In addition at intervals of one to several weeks felt faint with trembling of his head and dizziness.

Admitted to N.K. department when 4 years old. Eye examination normal. Left-handed. Head circumference 55 cm. Appeared quiet and sensible. Romberg: fell to the right. X-ray of skull: rather large skull with deep posterior fossa. E.E.G. not done.

V.E.G.: pressure 150, clear fluid. Ratio 0.29 (0.30/0.29). 3rd ventricle 6 mm. Temperature 38° C. the same day, normal two days later. Otherwise no complaints.

Follow-up: symptoms have quite disappeared. Has been in a treatment home on two occasions. Goes to an ordinary school and manages well though is somewhat restless. Continues to take phenobarbitone. Physical examination: normal, healthy appearance. Eye and neurological examination normal. Head circumference 56 cm. Motor system completely normal; is left-handed.

Diagnosis: healthy. Slight degree of nervousness.

Summary: boy whose mother had placenta praevia, and birth was 4 weeks premature by Caesarian section. Severe asphyxia present. Always unsteady gait and frequent episodes of trembling of the head and dizziness. V.E.G. at the age of 4 years showed a ratio of 0.29. At follow-up all symptoms had disappeared. He was doing well at school though was rather nervous.

18.

N.K. no. 02539/48. Boy born 15.1.48. No familial predisposition. Second of two children (between the two deliveries there were 7 miscarriages). No information on pregnancy. Delivery at normal time. Because of threatened intrauterine asphyxia Caesarian section was performed. Child had to have lobeline and pentazol. Birth weight 3750 g.

Symptoms: slow development especially physically. Admitted to R.H. Paediatric Depart-

ment at 7 months with rigidity of lower limbs. Subdural puncture showed a small amount of yellow fluid on the left side. Right side normal. Skull X-ray and eye examination normal.

Admitted to N.K. department when nearly 9 months old. Eye examination normal. Head circumference 45 cm. First finger turned into palm. Lower limbs rather rigid with ankle clonus. Slight rigidity of upper limbs. X-ray of skull: sutures slightly gaping and posterior fossa perhaps a little deep. Sub-dural puncture: no fluid on the left side. On the right side bloodstained fluid which later cleared.

S.E.G.: pressure 350. Clear fluid. Ratio 0.29 (0.29/0.29). 3rd ventricle 11 mm. Surface air corresponding to the Sylvian fissure. No complications after the examination.

Follow-up: was admitted to R.H. Paediatric Department for 4 months at the age of one year. Referred for State mental care. Eye examination: presumably blind. *E.E.G.*: severe dysrhythmia. Died at home at 20 months of age. Death certificate diagnosis: diffuse cerebral atrophy. Complications: oligophrenia, severe emaciation. Direct cause of death: paralysis of the heart.

Diagnosis: rigidity, oligophrenia, blindness.

Summary: boy who was delivered by Caesarian section because of threatened intra-uterine asphyxia. Rigidity and slow development. *S.E.G.* ratio 0.29. 3rd ventricle 11 mm. Cortical air corresponded to Sylvian fissure. Referred for State mental care. Died at home at 20 months.

19.

N.K. no. 09730c/52. Boy born 4. 8. 50. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3100 g.

Symptoms: three episodes of brief clonic convulsions at one and 3 months which were not accompanied by any rise in temperature and lasted less than 5 minutes. When about 4 months old he was admitted to an infectious diseases hospital with generalised febrile clonic convulsions of two hours' duration. During admission there were three left-sided convulsions and one right-sided. *E.E.G.* revealed a possible organic brain lesion.

First admitted to N.K. department when 6 months old. Eye examination normal. Head circumference 42.5 cm. Possibly decreased reaction of left lower facial nerve. Development almost normal. X-ray of skull normal.

S.E.G.: ratio 0.29 (0.29/0.29). 3rd ventricle 6 mm. Increased surface air on the left side. No fever or complications. After discharge because of chicken-pox, re-admitted at 8 months when *exploratory craniotomy* over the right hemisphere was performed. There was pronounced cortical atrophy with microgyri and somewhat broad sulci with increased sub-arachnoid fluid. The atrophy was most pronounced caudally and temporally. No post-operative complications.

Third admission to N.K. department at 18 months because of continuing unilateral clonic convulsions, usually right-sided. Eye examination normal. Head circumference 46 cm.

Fourth admission at 2 years, again because of convulsions. No mental development had taken place. Head circumference 46.5 cm. Right-sided arteriography performed. During this investigation the patient stopped breathing and there was threatened laryngeal oedema. No rise in temperature.

Follow-up: admitted to a State mental institution from 3 years until his death at 4 years 3 months in hyperpyrexia. I.Q. 43. Head circumference on admission 46.5 cm. Was totally incontinent and helpless, and had occasional febrile episodes. No convulsions except shortly after admission.

Diagnosis: oligophrenia (imbecility), epilepsy, ? cerebral hyperpyrexia.

Summary: boy who from the age of one month had clonic convulsions of short duration. *S.E.G.* at the age of 4 months showed a ratio of 0.29. *Exploratory craniotomy* at 8 months of age revealed pronounced cortical atrophy with microgyri. He was admitted to a State mental institution where he was completely helpless and had episodes of fever. He died there at 4 years 3 months.

20.

N.K. no. 07680/51. Boy born 16. 3. 41. Familial predisposition: eldest brother had congenital unilateral atresia of the auditory canal. Fourth of five children. Pregnancy and delivery normal. Birth weight 3000-3500 g.

Symptoms: fell off his bicycle when nearly 10 years old. Admitted to hospital with concussion and fracture of the base of the skull. Was unconscious for 3-4 hours. About 6 weeks after the injury his gait became uncertain and he became tired and quiet. He was also deaf on the left side.

Admitted to N.K. department at 10 years 4 months. Eye examination normal. Motor and mental development normal. Neurological examination normal. Otological examination: destruction of left labyrinth. X-ray of skull normal. E.E.G. not done.

S.E.G.: pressure 230. Ratio 0.29 (0.28/0.31). 3rd ventricle 2 mm. Temperature 38.2° C. the next day, otherwise no complaints.

Follow-up: completely healthy. Does full-time farm work. Went to an ordinary school until 14 years old. Is still deaf in the left ear. Never has a headache, dizziness or vomiting. Physical examination: head circumference 55 cm. Eye examination normal. Reflexes: generalised brisk tendon reflexes, but hardly pathological. No Babinski, no ankle clonus. Left-sided deafness.

Diagnosis: left-sided deafness, otherwise healthy.

Summary: boy with a familial predisposition to ear malformations. Following concussion and a fracture of the base of the skull his gait became unsteady and he seemed tired and quiet. S.E.G. at 10 years 4 months showed a ratio of 0.29. At follow-up he was entirely fit and carrying out a full-time job.

21.

N.K. no. 23176/55. Boy born 18. 9. 47. No known familial predisposition. First of two children. No information on pregnancy. Delivery 4 weeks late. Asphyxia for 2 hours. Birth weight 4500 g.

Symptoms: always retarded in development, particularly motor development. Admitted to hospital twice from 2-3 years of age. Patient was recommended for State mental care. Admitted to R.H. Paediatric Department at 5 years 5 months of age. There has been progress during admission and he has learnt to say single words. Severe degree of rigidity but no seizures. Eye examination normal. E.E.G. probably normal. X-ray of skull normal.

Admitted N.K. department at 7½ years.

V.E.G.: pressure 300. Ratio 0.29 (0.26/0.31). 3rd ventricle 5 mm. *Right-sided anaesthesia of globus pallidus* performed and about 14 days later *left-sided predunculectomy*. Immediately after operation right arm became paralysed with decreased muscle tone in hand and all extensor muscles. Temperature after examination and operation was 38.2° C. otherwise no complications.

Follow-up: rigidity almost unchanged after operation. Has continued to develop. Says more words now than previously. Is in a home for chronic sick children.

Diagnosis: rigidity. Intelligence difficult to assess but presumably almost normal.

Summary: a boy who was asphyxiated for two hours and was always retarded in development. V.E.G. at the age of 7½ years showed a ratio of 0.29, 3rd ventricle 5 mm. Right-sided anaesthesia of globus pallidus performed and left-sided pedunculotomy. His condition has remained almost unchanged. He is still very rigid and is in a home for chronic sick children.

22.

N.K. no. 01326/48. Boy born 19. 3. 41. Familial predisposition: mother and mother's family suffer from migraine. First of four children. Pregnancy normal. Delivery: severe pressure marks, otherwise nothing abnormal. Birth weight 3500 g.

Symptoms: when he was one year old had jactation of the head. Since two years of age unable to point at a given object. Later had headache, nausea and vomiting accompanied by sleepiness. This occurred 4 times a month. Admitted to R.H. Neuro-

medical Department. Temperature was always low (35–36° C.) and therefore a hypothalamic encephalitis or encephalopathy was considered.

Admitted to N.K. Department at 6 years 11 months. There was Steward-Holmes' sign on the left side. Skull X-ray normal. Eye examination normal. E.E.G. not done. Possibly a little backward.

V.E.G.: pressure 150. Ratio 0.30 (0.32/0.28). 3rd ventricle 5 mm. No complications.

Follow-up: the low temperature was found to occur only during seizures and there had been no similar attacks since discharge. Suffered from headaches at school. Left school two years ago. Now works in a machine factory and is doing well. Is slightly word-blind. Physically fit and an active sportsman. Physical examination: normal, healthy appearance. Head circumference 56.7 cm. Eye examination normal. Reflexes in upper extremities brisk. Patellar reflexes slightly brisker on the left. No ankle clonus or Babinski. Finger-nose and finger-finger tests normal.

Diagnosis: healthy.

Summary: a boy who at delivery had pressure marks but was otherwise normal. From the age of a year had jactation of head. Later had headaches, vomiting and drowsiness. *V.E.G.* at 6 years 11 months showed a ratio of 0.30, 3rd ventricle 5 mm. Has since had no trouble and development has been normal.

23.

N.K. no. 04177/49. Boy born 31. 8. 48. No familial predisposition. First of two children. Pregnancy normal. Protracted forceps delivery. Patient was black but cried straight away. Birth weight 3200 g.

Symptoms: between the age of 1–4 months he had numerous seizures lasting a few seconds during which he became stiff, bent his arms and legs and went blue. Admitted twice to a paediatric department. No further seizures. Development was poor and unquestionably retarded. At one year could only stand and sit with support.

Admitted to the R.H. Paediatric Department. X-ray of skull normal.

Admitted to N.K. department at the age of one year. Eye examination normal. Possibly slightly mongoloid in appearance. Alternating convergent squint. Bilateral Babinski. X-ray of skull: no definite abnormality. E.E.G. not done.

V.E.G.: pressure 80. Ratio 0.30 (0.32/0.29). 3rd ventricle 2 mm. Temperature 38.3° C. the day after. Brief post-operative malaise.

Follow-up: I.Q. at 4 years was 47. Admitted to a State mental institution at 6 years 3 months. Was severely mentally retarded and no contact could be made with him. A later report said that he did not respond very much. He chattered unintelligibly. Development was slow. At the age of 8 years he wandered about without being able to occupy himself with toys. Was not nearly so contrary as the beginning. Was toilet trained during the day. Physical examination: head circumference 49 cm. Small and thin and resembles a perinatally-damaged child. Does not look at the examiner. Understands nothing that is said to him. Is somewhat clumsy and stiff in his movements but neither spastic nor rigid. No hyperkinesia.

Diagnosis: oligophrenia (imbecility).

Summary: a boy who had a protracted forceps delivery after which he was black. Episodes of rigidity and cyanosis between 1–4 months and retarded development. *V.E.G.* at one year of age showed a ratio of 0.30, 3rd ventricle 2 mm. Is in a State mental institution and making no real progress. Movements somewhat clumsy and stiff.

24.

N.K. no. 23026/55. Boy born 29. 6. 41. No familial predisposition. Pregnancy and delivery normal. Birth weight 3500 g. Only child.

Symptoms: between the age of 7–9 years hurt his head three times. The first time there was brief loss of consciousness, the last time dizziness only. Headache in the occipital and temporal region with accompanying loss of memory for both recent and distant events. When 13 he did not feel very well at school; did not lose consciousness

but seemed withdrawn. Temperature 39°C . This was followed by similar attacks lasting from 15 minutes to an hour. No convulsions. Admitted to hospital where E.C.G. showed left-sided axis deviation.

Admitted to N.K. department at age of 13 years 8 months. Appeared normal mentally but memory a little reduced. I.Q. 98. Neurological examination normal. E.E.G. no definite abnormality (possible changes in the occipital region). X-ray of skull normal.

S.E.G.: pressure 325. Ratio 0.30 (0.33/0.28). 3rd ventricle 4 mm. Temperature 38.3°C . the same day, otherwise no complications.

Follow-up: has never been so well. No headache or seizures. Attends grammar school. There is only slight memory impairment. The patient was of a normal and healthy appearance.

Diagnosis: healthy.

Summary: a boy who from the age of 7-9 years hurt his head on three occasions with loss of consciousness once. Following this he had headache and impairment of memory. *S.E.G.* at the age of 13 years 8 months showed a ratio of 0.30. At follow-up he was perfectly well and physical examination revealed no abnormality.

25.

N.K. no. 2847/41. Girl born 5.5.28. Familial predisposition: sister had had a single generalised convulsion. Second of four children. Pregnancy and delivery normal, but delivery followed by jaundice of unknown duration.

Symptoms: when about 4 years old had a single episode of automatism. From the age of 10 had generalised convulsions with loss of consciousness occurring several times daily at intervals of a few months. In the last 6 months psychological difficulties in relation to friends and family, and for the last 3-4 months episodes of petit mal. Admitted to R.H. Neuromedical Department.

Admitted to N.K. department when 13 years 5 months old. Eye examination and neurological examination normal. X-ray of skull: medium sized, thin-walled. E.E.G. not performed.

V.E.G.: ratio 0.31 (0.29/0.33). 3rd ventricle 7 mm. Slight headache for a few days following the examination and temperature of 38°C . the same day.

Follow-up: admitted to a hospital for epileptics from the age of 14 to 18 years with a diagnosis of cryptogenic epilepsy. Did well in school but had periodic difficulties with school friends. E.E.G. when 14 years old showed severe generalised dysrhythmia. L.E.G. when 17 years old showed a normal distribution of surface air. Ventricular system well-filled, slight dilatation of the left lateral ventricle including left temporal horn. 3rd ventricle possibly a little widened. Later placed under family care and did very well. Patient had been traced through the population register and it is known that she has married at least three times and changed addresses approximately 15 times. Unfortunately she failed to answer several questionnaires.

Diagnosis: epilepsy (? now ceased). Presumably healthy.

Summary: girl whose sister had a single convulsion and who had neonatal jaundice of unknown duration. From 10 years of age generalised convulsions of varying frequency. From 13 years of age had petit mal. *V.E.G.* ratio when 13 years 6 months 0.31. In a hospital for epileptics for 4 years where she did well. It is known that she has been married at least three times but she has failed to answer all enquiries.

26.

N.K. no. 8242/46. Girl born 25.4.43. No known familial predisposition. Only child. Pregnancy and birth normal. Birth weight approximately 3500 g.

Symptoms: when about 3 years old sustained a possible head injury, and during the following week severe right-sided paresis became apparent in legs. Admitted to R.H. Paediatric Department where a left-sided nystagmus was found.

Admitted to N.K. department at 3 years. Eye examination normal. Severe right-sided spastic hemiplegia. X-ray of skull showed increased digital markings and possibly slight diastasis. E.E.G. not done.

V.E.G.: pressure 160. Ratio 0.31 (0.30/0.33). 3rd ventricle 3 mm. Temperature 37.9° C. the same day, otherwise no complications.

Left-sided arteriography showed normal conditions.

Follow-up: has never had seizures. Attends grammar school and is doing well. Hemiparesis has been gradually decreasing year by year. Writes with right hand but prefers left. Mental state completely normal. Physical examination: normal, healthy appearance. Head circumference 56 cm. Eye examination and neurological examination normal.

Diagnosis: healthy.

Summary: girl who after a possible head injury at the age of 3 years developed right-sided hemiplegia. *V.E.G.* showed a ratio of 0.31. 3rd ventricle 3 mm. *Follow-up* showed that the hemiparesis had been gradually decreasing over the years and the intellectual development had been completely normal.

27.

N.K. no. 0588/47. Boy born 8.7.46. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3625 g.

Symptoms: at the age of 6 months he was flaccid. Treated with calcium and cod liver oil with good effect. When one year old he had an episode of prolonged vomiting and was admitted to an infectious diseases hospital with a diagnosis of gastroenteritis, constipation and anaemia. He was restless, miserable and noticeably flaccid and apathetic with a temperature of 38° C. Admitted to a paediatric department at 15 months of age. Eye examination and skull X-ray normal.

Admitted to N.K. department at 15 months of age. Eye examination normal. He lay on his back with his head turned to the right. Muscle tone decreased especially in the lower limbs. Normal reflexes. Skull X-ray: somewhat deep posterior fossa. *E.E.G.* not done.

V.E.G.: pressure 110. Ratio 0.31 (0.32/0.30). 3rd ventricle 18 mm. No complications after the examination.

Follow-up: was examined in the R.H. Paediatric Department at 18 months of age. At that time admission was arranged but shortly afterwards the patient made a spontaneous recovery and since then has been entirely well. He started to walk at the age of 2 years. Attends a normal school and is in the right class for his age. Physical examination: healthy appearance. Head circumference 54 cm. Eye and neurological examination normal. Pronounced enamel defect in the permanent front teeth. Mentally normal.

Diagnosis: healthy. Enamel defect in front teeth.

Summary: boy who was flaccid at 6 months of age. When one year old had an episode of prolonged vomiting after which he was flaccid and apathetic. *V.E.G.* at 15 months of age showed a ratio of 0.31. Made a spontaneous recovery between 18 months and 2 years of age, and since then has been healthy.

28.

N.K. no. 02666/48. Boy born 7.7.38. No familial predisposition. Last of ten children. No information on pregnancy. Delivery normal. Birth weight unknown.

Symptoms: left-sided radical mastoidectomy at the age of 7 years. Admitted to hospital at the age of 10 years for right-sided cholesteatoma operation, followed by right-sided radical mastoidectomy and resection of cavum tympanum. Bleeding from a dural artery was treated by compression and suture. Sub-febrile for 5 weeks with nausea, occasional vomiting and abdominal pain. Headache of 4 days' duration accompanied by faintness and nausea. Lumbar puncture revealed slightly bloodstained fluid with no cells.

Admitted to N.K. department at 10 years 4 months. Eye examination normal. Otolological examination revealed sequelae of bilateral operations and reduced hearing. Neurological examination normal. X-ray of skull normal. Sub-occipital puncture: clear fluid, possibly with slight xanthochrome colouring. *E.E.G.* not done.

S.E.G.: pressure 90. Clear fluid. Incomplete filling of the system.

V.E.G.: pressure 100. Clear fluid. Ratio 0.31 (0.29/0.33). 3rd ventricle 5 mm. Temperature 38° C. the following day, otherwise no complaints.

Follow-up: no further admissions to hospital after last discharge. No headache, eye symptoms or similar troubles. Continues to be very deaf but manages an ordinary conversation fairly well. Has done farm work for 4 years and according to his employer is of average ability. Can occasionally be rather stubborn. Plays football well. Physical examination: normal, healthy appearance. Head circumference 58.4 cm. Neurological examination normal. Walks, runs and talks well but has some impairment of hearing.

Diagnosis: decreased hearing, otherwise well.

Summary: boy who at 7 and 10 years had radical ear operations. Admitted to N.K. department at 10 years 4 months. V.E.G. showed a ratio of 0.31. 3rd ventricle 5 mm. Follow-up: had been perfectly well since discharge except for reduced hearing.

29.

N.K. no. 03300/49. Girl born 12.4.38. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight just under 3000 g.

Symptoms: at 8 years sustained a head injury without loss of consciousness. At 10 years further head injury during gymnastics with possible momentary unconsciousness. Kept in bed for two weeks. Headache during year before admission. During the 6 months before admission felt pressure at the back of the head, followed by nausea and vomiting. This occurred at intervals of 2-4 weeks and was accompanied by pallor but not by seizures. Had become less energetic, was irritable and sensitive to noise. Did well at school, but had not done any reading for two months.

Admitted to N.K. department at age of 11 years. Normal, healthy appearance. Eye examination normal. Neurological examination: reflexes normal. Slight inaccuracy of finger-nose test. X-ray of skull normal. E.E.G. showed severe dysrhythmia with left-sided predominance.

V.E.G: pressure 0. Ratio 0.31 (0.31/0.31). 3rd ventricle 4 mm. Temperature 38.8° C. same day, normal third day. Otherwise no complaints.

Follow-up: since examination in N.K. department has been well. Has had a single episode of rapid pulse and symptoms similar to those she had earlier; this occurred three months after discharge and she has since had no further attacks. Has taken secondary school leaving examination and since lived for some years abroad because of sinusitis. Is now back studying to be a teacher and is doing well. Physical examination: patient is small in size. Head circumference 55 cm. No neurological abnormality present.

Diagnosis: healthy.

Summary: a girl who at 10 years of age sustained a head injury with possible brief loss of consciousness. In the following 6 months had episodes of pallor, headache, nausea and vomiting and increasing irritability. V.E.G. at 11 years showed a ratio of 0.31. 3rd ventricle 4 mm. At follow-up, except for a single episode 3 months after discharge, she had been perfectly well.

30.

N.K. no. 05350/50. Boy born 3.8.47. No familial predisposition. Third of four children. No information on pregnancy. Delivery about 4 weeks premature. Birth weight 2400 g.

Symptoms: was flaccid and cyanotic for some days after birth. Development always retarded. On admission at the age of 2½ could not walk without support. Was rather restless. Understood most of what was said but said nothing.

Admitted to N.K. department at age of 2½. Mongoloid appearance. Eye examination normal. Appeared feeble-minded. Walked well holding on to furniture and was continuously active. Reflexes normal. X-ray of skull: thin cranial bones with open anterior fontanelle. E.E.G. not done.

S.E.G: pressure 250. Slightly bloodstained fluid. No air in the ventricular system.

V.E.G: pressure 140. Ratio 0.31 (0.33/0.29). 3rd ventricle 7 mm. No cortical air. Temperature after first examination 38° C. and after the second 39° C. Otherwise no complaints.

Follow-up: admitted to State mental institution at 4½ years. Diagnosed as a mongoloid idiot. I.Q. 44. During his stay there he has been an unusually good, peaceful and contented little fellow. Understands what is said to him. Is toilet trained and beginning

to talk but speaks indistinctly. Physical examination: mongoloid child with epicanthus and partial "4 finger line". Large thumb and short fat fingers, especially the first and fifth. Happy and very trusting. Head circumference 50.4 cm. No reflex changes. Motor ability normal.

Diagnosis: oligophrenia (mongoloid type).

Summary: boy who was flaccid and cyanotic at birth which was said to be 4 weeks premature. Development always retarded. On admission at 2½ years to N.K. department found to be of mongoloid appearance. V.E.G. showed a ratio of 0.31. 3rd ventricle 7 mm. Is in a State mental institution and doing well.

31.

N.K. no. 6791/51. Boy born 23.2.47. No familial predisposition. Only child. Pregnancy: fainting in the 4th month, otherwise no abnormality. Delivery normal. Birth weight 3800 g.

Symptoms: 9 months before admission hit the back of his head without apparent concussion. Six months before admission had attacks resembling petit mal. On New Year's Day 1951 admitted to a paediatric department unconscious after convulsion involving right side of face and accompanying brief generalised convulsions. Might possibly have fallen just beforehand. E.E.G. showed focus of spike-waves in the left occipital region and a focus of slow activity in the right temporal region. X-ray of skull normal.

Admitted to N.K. department at 4 years. Eye examination normal. Head circumference 52.5 cm. Plantar responses atypical.

S.E.G.: pressure 300. Clear fluid. Ratio 0.31 (0.31/0.30). 3rd ventricle 3 mm. No increase of surface air. Temperature 38.2° C. the day after examination, otherwise no complaints.

Follow-up: had right-sided convulsion at 4 years 10 months. This was followed by periodic severe headaches and attacks of petit mal. Treated with phenobarbitone until age of 9 years. E.E.G. done one year later showed normal conditions. Stammers slightly. Never has headache. Is doing very well in a particularly demanding school. Physical examination: looks very well. Head circumference 55 cm. Eye and neurological examination normal. Speech almost normal.

Diagnosis: healthy, previous epilepsy, slight stammer.

Summary: a boy who at the age of 3¼ years sustained a head injury. Three months later he developed seizures resembling petit mal. Admitted at age of 4 years after brief generalised convulsions. S.E.G. ratio 0.31. 3rd ventricle 3 mm. At follow-up he had had a right-sided convulsion followed later by headache and occasional attacks of petit mal. Much improved over the last few years and now only stammers slightly.

32.

N.K. no. 09185a/52. Boy born 21.6.41. No familial predisposition. First of three children. Pregnancy and delivery normal. Birth weight 3750 g.

Symptoms: from the age of 6, over a couple of years, episodes of bad temper, irritability and headaches. When 9½ years old he had a head injury in a traffic accident with loss of consciousness for 48 hours. Was admitted to hospital where a small cranial fracture was found and possible intracranial haemorrhage. Since then had had frequent headaches localised to the forehead accompanied by vomiting, dizziness, sensitivity to noise and difficulties with school work. No convulsions.

First admitted to N.K. department when 10 years 3 months old. Thin but otherwise normal. Head circumference 53 cms. Eye examination and neurological examination normal. Skull X-ray normal. E.E.G. showed moderate diffuse dysrhythmia, most pronounced occipitally.

S.E.G.: pressure 180. Ratio 0.31 (0.32/0.30). 3rd ventricle 5 mm. Normal distribution of surface air. Temperature 38.2° C. the day after examination and headache for a few days.

Second admission to N.K. department when nearly 11 years old. Headaches had increased and he had changed psychologically. He had attacks of uncontrollable anger, was irritable, teasing, spiteful and domineering. His memory had deteriorated and there was

enuresis and encopresis. Physical examination: eye and neurological examination normal. E.E.G: moderate dysrhythmia with abnormal findings in some areas, chiefly in the left hemisphere and particularly occipitally.

V.E.G: pressure 0. Ratio 0.32 (0.33/0.32). 3rd ventricle 6 mm. Temperature 38.2° C. the same day, otherwise no complications.

Left-sided arteriography: mid-way the anterior cerebral artery made an approximately 2 cm. deep bend to the left possibly due to a septum pellucidum cyst.

Follow-up: for some years the patient was very nervous and suffered from headaches and uncontrollable affect reactions. He did not enjoy school and was teased a great deal. From the age of 13½ he was taught at home and got on very much better. Headaches only occur once or twice a month and he is much less nervous. In addition to his school work he delivers groceries. His headaches are rarely accompanied by vomiting and seem only to occur when he is overtired. Physical examination: head circumference 54 cm. Reflexes and eye examination normal. Psychological development corresponds to his age.

Diagnosis: headache (constitutional and post-concussional).

Summary: boy who aged 9½ sustained head injury with 48 hours' loss of consciousness. Since then has had headache and accompanying complaints. S.E.G. at 10 years of age: ratio 0.31. Repeated examination when almost 11 years old because of increasing headache and temper tantrums showed V.E.G. ratio to be 0.32. At follow-up he had been much better since he had been taken away from school, and his headaches occurred only rarely.

33.

N.K. no. 08586/52. Boy born 27. 8. 51. Familial predisposition: father, father's sister and father's father had all undergone splenectomy because of a blood disorder. Only child. Pregnancy normal. Delivery 6 weeks premature. No asphyxia. Birth weight 1850 g.

Symptoms: admitted immediately after birth because of alternating rigidity and flaccidity together with cyanosis. Was jaundiced from the third day until he was about two weeks old. Improved and was very well on discharge two months later. Since had a tendency to cyanosis and spells of crying with accompanying rigidity. Pale and tired after attack. Admitted to R.H. Paediatric Department at age of 5 months. X-ray of skull and E.E.G. normal. Sub-dural puncture revealed clear fluid on the left side.

Admitted to N.K. department at 5 months. Sub-dural puncture revealed no fluid on the right side, clear fluid on the left. Head in opisthotonus position. Head circumference 41 cm. Eyes normal apart from slight intermittent squint. Could not hold his head up or focus. E.E.G. not done.

V.E.G: pressure 180. Ratio 0.31 (0.29/0.32). 3rd ventricle 4 mm. No surface air. No complications after examination.

Follow-up: has since discharge been an out-patient in the R.H. Paediatric Department. Often assumes opisthotonus position, is frequently febrile and has convulsions. From about 2 years of age athetoid tongue movements were noticed. Admitted to State mental institution at the age of 2 years. Could not stand, walk, talk or help himself in any way. Died the day after admission with a high temperature. At the inquest the diagnosis was given as pulmonary oedema and stasis, acute emphysema, acute stasis of the organs, petechiae of the thymus, pericardium and pleura, hypertrophy of the left tonsil and megalo-oesophagus. Microscopy revealed no sign of infection. Immediate cause of death therefore unknown. Brain autopsy revealed congenital cerebral dysplasia, dysmyelination of globus pallidus, cerebral hyperaemia and oedema, hypothalamic encephalitis which could possibly have been cause of hyperpyrexia.

Diagnosis: oligophrenia, rigidity, epilepsy.

Summary: boy with a paternal family history of a blood disorder. Was born 6 weeks prematurely and immediately after birth had alternating rigidity and flaccidity and later cyanosis. V.E.G. at 5 months of age: ratio 0.31. 3rd ventricle 4 mm. After this he had an increasing number of febrile episodes accompanied by convulsions. Admitted to a State mental institution at the age of 2 years and died the day following admission in hyperpyrexia.

34.

N.K. no. 21287/53. Girl born 15. 3. 53. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3750 g.

Symptoms: in first 24 hours of life had large blue pressure marks over right temple. From the age of one month had generalised convulsions increasing in frequency until they occurred twice daily. Development presumably retarded. Admitted to R.H. Paediatric Department 6 months of age. E.E.G. abnormal during seizure. X-ray of skull normal. Psychological examination showed development to correspond to 2-3 months.

Admitted to N.K. department at 7 months of age. Eye examination normal. Neurological examination showed no definite abnormality. X-ray of skull: peculiar shaped skull without foramen magnum impressions.

S.E.G.: pressure 250, clear fluid. Ratio 0.31 (0.31/0.31). 3rd ventricle 7 mm. Increased cortical air frontally, most pronounced on the left side. Temperature 37.8° C. the day after the examination, otherwise no complications.

Follow-up: recommended for State mental care (developmental quotient at one year was 22) and admitted to State mental institution for 3 months at age of 3 years. Head circumference 46 cm. Somewhat flaccid and could not use her legs at all. Convulsions increased. Developed chicken-pox and this was followed by still more convulsions and a high temperature which failed to respond to antibiotics and ended in death. No autopsy performed. Death certificate diagnosis: chicken-pox, hyperpyrexia, severe epilepsy.

Diagnosis: oligophrenia (idiocy), epilepsy.

Summary: a girl who had blue pressure marks at birth and generalised convulsions from one month of age together with retarded development. S.E.G. at 7 months showed a ratio of 0.31, 3rd ventricle 7 mm. Increased cortical air present frontally. At follow-up she had been admitted to a State institution where she had died following chicken-pox.

35.

N.K. no. 22192/54. Girl born 27. 6. 46. No familial predisposition. Only child. Pregnancy normal. Delivery lasted several days. Slightly jaundiced during the first days of life. Birth weight 3700 g.

Symptoms: fine constant nystagmus since infancy. Development normal. Had a number of minor head injuries without particular symptoms during childhood. Periodic headache for some years, localised to the left side of the forehead.

Admitted to N.K. department at age of 8 years. Eye examination showed horizontal, fine nystagmus and hypermetropia. X-ray of skull: thin and dolichocephalic with deep posterior fossa. E.E.G. normal.

S.E.G.: pressure 300, clear fluid. Ratio 0.31 (0.31/0.31). 3rd ventricle 8 mm. No increase of surface air. No complications after examination.

Follow-up: has been well since examination and has no headache. Nystagmus unchanged. Is in the normal class at school and never has convulsions. Physical examination: nystagmus unchanged. Otherwise normal, healthy appearance. Head circumference 54.4 cm. Reflexes normal.

Diagnosis: nystagmus, otherwise healthy.

Summary: girl who since infancy had had a fine, horizontal nystagmus, and later suffered from periodic headache localised to the left side of the forehead. S.E.G. ratio 0.31. At follow-up she was completely well except for the unchanged nystagmus.

36.

N.K. no. 23088/55. Boy born 25. 1. 42. No familial predisposition. Only child. Pregnancy normal. Delivery protracted, rupture of membranes two days beforehand. Patient swallowed amniotic fluid but was not asphyxiated. Birth weight 3500 g.

Symptoms: between 10 and 11 years of age sustained several minor head injuries without loss of consciousness. Since developed headache. At 12 years of age admitted to hospital because of febrile episodes and epistaxis. At 13 years tonsils were removed. Was difficult to rouse after anaesthetic and felt unwell for some time afterwards. Shortly after this a left-sided convulsion occurred.

Admitted to N.K. department at age of 13 years. Eye examination normal. Reflexes normal. X-ray of skull: rather large and circular, otherwise normal. E.E.G: no side difference. Small spikes in the left temporal region. I.Q. 112. Right-sided arteriography: normal.

S.E.G: pressure 280. Ratio 0.31 (0.33/0.29). 3rd ventricle 5 mm. Temperature 37.8° C. after arteriography and after an earlier attempt at S.E.G. No temperature after the last attempt.

Follow-up: for a while after discharge continued to be rather nervous and odd. Would wake up and shout: "This is ether". No convulsions for a considerable number of years. Attends high school at his own wish. Plays a lot of handball. Has had a febrile episode without accompanying convulsion. Continues to take phenobarbitone. Physical examination: head circumference 55 cm. Healthy, normal appearance. Eyes normal, reflexes normal. Physically and mentally completely normal.

Diagnosis: healthy.

Summary: boy who had a difficult delivery. Between the age of 10 and 11 years he sustained several minor head injuries and at 13 had a left-sided convulsion following anaesthesia. S.E.G. ratio 0.31. 3rd ventricle 5 mm. At follow-up it emerged that after a period of nervousness following his discharge from hospital he improved and is now doing well at school.

37.

N.K. no. 23264/55. Boy born 17. 2. 54. No familial predisposition. Only child. Pregnancy normal. Delivery difficult with asphyxia. Birth weight 2400 g.

Symptoms: when 3 days old had generalised convulsions after which he was admitted to a paediatric department. Remained in hospital until the age of 4 months, and re-admitted from 7-9 months of age because of convulsions and loss of consciousness. Again admitted to hospital when nearly one year old because of convulsions and projectile vomiting. Developed slowly since then. E.E.G. at one month showed much irregular activity, and at 4 months a few abnormalities. Repeat E.E.G. at 7 months showed severe dysrhythmia of the "hypsarrhythmia" type. Skull X-ray normal. L.E.G. at 1 year 2 months: ratio 0.29 (0.27/0.30). 3rd ventricle: 3 mm. Surface air normal.

Admitted to N.K. department at 14 months: eye examination revealed bilateral atrophy of the optic nerve. Head circumference 43 cm. He made no attempt to stand and made athetoid movements of the head with sucking and grimacing. Moderate spastic tetraplegia with scissor position of the legs. Hyperactive reflexes, no Babinski. E.E.G. not performed on this admission.

V.E.G: pressure 150. Clear fluid. Ratio 0.31 (0.30/0.32). 3rd ventricle 4 mm. Temperature 38.5° C. Otherwise no complications. Cortical biopsy revealed no abnormality.

Follow-up: admitted to a State mental institution when 22 months old. No seizures. Physical examination: in fairly good general condition. Head circumference 44.8 cm. No eye symptoms, hyperkinesia or abnormal reflex findings. Only makes sounds but understands much of what is said to him.

Diagnosis: oligophrenia (? degree), "hypsarrhythmia", microcephaly.

Summary: boy whose birth was difficult with asphyxia. Generalised convulsions occurred from the age of 3 days. Developed slowly since. Abnormal E.E.G. of "hypsarrhythmia" type. V.E.G. at 15 months showed a ratio of 0.31. Is placed in a State mental institution. No convulsions. Microcephalic.

38.

N.K. no. 2646/41. Boy born 11. 8. 31. No familial predisposition. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: between the age of 5-6 years injured his head three times with no loss of consciousness. At the age of 6 years had a single seizure with right-sided facial contractions, motor aphasia and salivation. During the 2-3 years prior to admission periodic headache and dizziness. At 8 years of age transient left-sided loss of vision. During 9 months before admission had 30 seizures, occurring in groups and usually at night, accompanied by predominantly left-sided facial contractions. The right hand became

stiff, there was aphasia and salivation but no loss of consciousness. Five months before present admission there was transient diplopia. Admitted to R.H. Neuromedical Department at 8 years of age with a diagnosis of post-traumatic epilepsy. Readmitted at 8 years 4 months.

Admitted to N.K. department 8 years 4 months. A few scars present on the left side of the head. Eye examination normal. Patellar reflexes brisk. No Babinski. Skull X-ray showed it to be large and thin with increased venous grooves. Cranially on the left side there was possible hyperostosis. E.E.G. not performed.

V.E.G.: normal pressure. Ratio 0.32 (0.32/0.33). 3rd ventricle 6 mm. Temperature 38.2° C. on the same day. Otherwise no complications.

Second admission to N.K. department at 9 years 9 months of age. Over the last 15 months he had had 2-4 seizures each month with frequent right-sided frontal headache just before the convulsion. X-ray of the skull showed no definite abnormality. No seizures seen during admission.

Follow-up: anti-epileptic medicine had been discontinued at the age of 12-13 years, and his last seizures had occurred the night before his confirmation at the age of 14. The pressure frontally and above the eyes disappeared spontaneously at that time. When 21 he sustained a head injury and concussion during a bicycle race. This accident was not followed by any seizures or by headache. Is married and manages to do hard physical work without difficulty. Physical examination: appears healthy. Head circumference 57 cm. Eye and neurological examination normal.

Diagnosis: healthy.

Summary: boy who sustained head injuries between the age of 5-6 years. At the age of 6 years had a seizure with muscular contractions of the face followed by aphasia and salivation. *V.E.G.* at 8 years 4 months showed a ratio of 0.32. Continued to have seizures until the age of 14 years since which time he has been perfectly well in spite of a fairly serious head injury at 21 years of age.

39.

N.K. no. 4044/43. Boy born 1.4.30. No familial predisposition. Third of three children. Pregnancy normal. Delivery fast but otherwise normal. Birth weight 3125 g.

Symptoms: right-sided hemiplegia since birth. At 3 days had generalised tonic convulsions with loss of consciousness. Decreased over the next few years but increased again from the age of 10 years. Motor development and development of intelligence slow.

Admitted to N.K. department when almost 13 years old. Imbecile. Eye examination: slight temporal pallor of the optic discs. Right-sided spastic hemiplegia. Skull X-ray thin and brachycephalic with a protrusion corresponding to the right parietal region. E.E.G.: a number of formations of long duration over the whole cortex with pronounced dysrhythmia in both frontal regions.

S.E.G.: clear fluid. Ratio 0.32 (0.30/0.34). 3rd ventricle 4 mm. Small amount of surface air. Temperature 38° C. on the same day, otherwise no complications.

Follow-up: since the age of 5 years has been under State mental care at home. I.Q. at 9 years of age 38. Tendency to convulsions practically unchanged since admission. Has had some home education and is a "scout". Has some speech difficulties. Can run simple errands but does not like doing any real work in his father's shop. Looks after himself without difficulty. Physical examination: head circumference 55.5 cm. Right-sided spastic hemiplegia of moderate severity. Right-sided ankle clonus and Babinski sign. Ankle clonus also present on left side but plantar responses normal. Appears happy and contented. It is difficult to understand his speech but he understands what is said to him fairly well and is very co-operative.

Diagnosis: oligophrenia (imbecilitas), epilepsy, right-sided spastic hemiplegia (tetra-plegia, right side more involved than left).

Summary: boy whose delivery was fast and who, since birth, has had right-sided spastic hemiplegia and generalised convulsions since the third day of life. Always retarded intellectually and in his motor development. *S.E.G.* at 12 years 10 months showed a ratio of 0.32. Lives at home and still has seizures. Looks after himself well.

40.

N.K. no. 4339/43. Girl born 13.9.36. Familial predisposition: father's sister died at the age of one year of "teething convulsions." Father's brother died at 9 years from a brain disorder. Patient is first of two children. Pregnancy was characterised by severe vomiting for almost 6 months and accompanying loss of weight. Delivery was by breech presentation and asphyxia was present. Birth weight 3250 g.

Symptoms: early development normal. Convulsions began at 2½ years of age, usually right-sided but occasionally generalised. Often precipitated by fever and increasing in frequency. Admitted to R.H. Paediatric Department at 2½ years of age.

Admitted to N.K. Department at 6 years 8 months. Eye examination normal. Right-sided Babinski. X-ray of skull: brachycephaly. Cranial bones thin with deep posterior fossa. E.E.G: severe dysrhythmia, spike-waves.

S.E.G: pressure 140. Ratio 0.32 (0.29/0.34). 3rd ventricle 4 mm. Temperature of 38.4° C. the day following the examination, becoming normal on the third day.

Follow-up: stayed in a hospital for epileptics for 2 months, and was re-admitted at the age of 18 years. There had been a number of behaviour difficulties at home principally due to lack of discipline. Grand mal seizures had continued but were not severe and there were long free intervals. During admission to the hospital for epileptics S.E.G. (18 years of age) showed a ratio of 0.34 (0.32/0.36), 3rd ventricle 5 mm. No surface air. The patient was not personally examined by the author but information was obtained through detailed discussion with her mother. She failed to reach grammar school standard. After a long seizure-free period following her last admission to hospital, seizures recurred because she discontinued her medicine. She had several domestic posts and held such a position in England. Attended a domestic science school and did very well. The impression gained is that the patient is doing well apart from the tendency to seizures and from pictures of her she appears to be a healthy and normal looking young woman.

Diagnosis: epilepsies, behaviour difficulties.

Summary: girl with paternal familial predisposition to neurological disorders. Pregnancy complicated by severe vomiting and delivery was by breech presentation with asphyxia. Convulsions from the age of 2½ years, usually right-sided. S.E.G. ratio at 6½ years 0.32. Repeated S.E.G. at the age of 18 years 0.34. Seizures continued but less frequently over the last few years. Had had some behaviour difficulties but is now doing well in domestic posts.

41.

N.K. no. 01629/48. Boy born 26.11.47. Familial predisposition: several distant relatives have had spinal disorders. Pregnancy normal. Delivery accelerated by quinine and pituitrin. Birth weight 4280 g.

Symptoms: would not suck. At two months of age it was noticed that the patient's development was very delayed. He did not smile or react to light or sound. At 3 months of age he had convulsions with flexion of the right arm and leg and extension of the left arm. The attacks varied from 3–20 daily. Investigated in England where mental defect and slight left-sided hemiparesis was found.

Admitted to N.K. department at 5 months. Healthy appearance but development retarded. Eye examination normal. Head circumference 42.5 cm. with "cracked pot" sound on cranial percussion. Atypical bilateral Babinski. X-ray of skull normal.

V.E.G: pressure 250. Ratio 0.32 (0.31/0.33) 3rd ventricle 7 mm. Temperature 38.7° C. the day after, normal on the third day. Otherwise no complaints.

Follow-up: after discharge the patient was admitted to the hospital for epileptics and from there went home to England. He died six months later from pneumonia. No other information obtainable.

Diagnosis: oligophrenia, ? degree, epilepsy.

Summary: boy in whose family several distant relatives had spinal disorders. At two months of age he was seen to be retarded. He then began to have increasing convulsions. At 5 months of age V.E.G. showed a ratio of 0.32, 3rd ventricle 7 mm. Died six months later at home from bronchopneumonia.

42.

N.K. no. 03853/49. Girl born 14. 7. 44. Familial predisposition not known; is an adopted child. Pregnancy: nothing known. Delivery 2-3 weeks premature. Birth weight 2800 g.

Symptoms: squint since the age of 8 months. Minor head injury at the age of 2 years. At 4 years had a convulsion involving the right arm and leg. No loss of consciousness. After the convulsion had left-sided paresis which lasted about 30 minutes. Four months prior to admission while in kindergarten had a similar attack followed by loss of consciousness for 5 hours and left-sided paralysis. Admitted to hospital and anti-epileptic treatment started. Three months before admission had a minor convulsion localised to the left leg and foot lasting only a few minutes. Health had been generally affected and the patient had been very bad tempered.

Admitted to N.K. department at age of 5 years. Eye examination: alternating convergent squint. Neurological examination normal. X-ray of skull showed it to be large and thin-walled with increased markings and clear venous grooves. E.E.G.: many low frequencies, chiefly on the right side.

S.E.G.: pressure 150. Ratio 0.32 (0.32/0.32). 3rd ventricle 3 mm. Some surface air on the left side but not very pronounced. None on the right side. Temperature 38.6° C. on the third day, thereafter normal. Otherwise no complaints.

Follow-up: admitted to epileptic hospital after discharge and for a short while had mild seizures. Since measles with fever to 40° C. at the age of 6 years has been seizure-free. Attends grammar school and is doing very well. Finds arithmetic rather difficult but this does not bother her very much. Continues with anti-epileptic treatment. Physical examination: normal, healthy appearance, corresponding to age. Head circumference 56.5 cm. Eye examination normal. Neurological examination showed brisk patellar responses on both sides, but hardly pathological, and on ankle clonus test there were unsustained jerks on the left side but not on the right. Plantar reflexes normal. Appears completely normal.

Diagnosis: healthy, previous epilepsy.

Summary: girl who since 8 months of age had a squint. Minor head injuries occurred at 2 years and right-sided convulsion followed at 4 years with subsequent transitory paresis. Later minor convulsions prior to admission. S.E.G. at 5 years showed a ratio of 0.32. 3rd ventricle 3 mm. After an attack of measles accompanied by high fever the convulsions ceased. Is now doing well, goes to a normal school.

43.

N.K. no. 06665/50. Girl born 14. 11. 48. No familial predisposition. Third of three children. Pregnancy normal. Delivery difficult, lasting 20 hours. No asphyxia. Birth weight 3750 g.

Symptoms: immediately after birth it was noticed that the legs and specially the ankles were hyperextended. Began to walk at the age of 18 months with stiff extended legs. When 2 years old fell off kitchen table and this was followed by slight headache. Gait difficulties increased with equinus deformity.

Admitted to N.K. department at 2 years of age. Legs stiff. Severe spastic paraparesis present. Lumbar myelography showed normal filling.

S.E.G.: the following day showed a pressure of 270, clear fluid. Ratio 0.32 (0.32/0.33). 3rd ventricle 10 mm. Moderate amount of surface air on the right side. During the 24 hours following the examination there was a sharp rise of temperature with many brain stem seizures, and the patient died in hyperpyrexia. Autopsy not permitted.

Diagnosis: spastic paraplegia, hyperpyrexia.

Summary: a girl who immediately after birth was noticed to have extended legs and later showed gait difficulties. S.E.G. showed a ratio of 0.32. 3rd ventricle 10 mm. During the 24 hours after the examination there was a sharp rise of temperature together with brain stem seizures. Death followed.

44.

N.K. no. 07313a/51. Girl born 14. 11. 40. No familial predisposition. First of three children. Pregnancy and birth normal. Birth weight 3750 g.

Symptoms: when 6 months old fell in day nursery but had no symptoms. When 3

years old had brief left-sided convulsions which increased in frequency. They began with jerks in the arm and were followed by clonic jerks in the leg and face. No loss of consciousness. Mental development normal. Did well at school. Admitted to a neurological department at 7 years of age. E.E.G. showed a focal organic lesion in the right hemisphere. L.E.G. described as normal. E.E.G. in a paediatric department at 10 years of age showed a focus posteriorly in the right hemisphere.

Admitted to N.K. department at 11 years of age. Eye examination normal. Mental development normal. Reflex examination showed slight paresis of the left arm. X-ray of skull normal. E.E.G. showed severe abnormality with changes localised to the right hemisphere.

S.E.G.: pressure 370, clear fluid. Ratio 0.32 (0.34/0.31). 3rd ventricle 3 mm. Temperature 38.1°C . the day after examination, otherwise no complications. Shortly after S.E.G. right-sided arteriography was performed and this showed no definite abnormality. Temperature 37.8°C . the day after with swelling of the throat, otherwise no complications.

Operation over right hemisphere. Downwards in the post-central region a small sunken area was found. No really well-defined focus was seen on E.E.G. so further exploration was not carried out. No post-operative complications apart from a temperature of 38.7°C . on the following day.

Second admission to N.K. department 3 months later. In two months had had a total of 6 left-sided seizures. No petit mal. Seizures were not severe and occurred only in the morning. Eye and neurological examination normal. E.E.G. showed moderately severe dysrhythmia localised to the right hemisphere. Further examinations not carried out. E.E.G. carried out as an out-patient remained almost unchanged until the age of $14\frac{1}{2}$ when it appeared less abnormal than before.

Follow-up: is doing fairly well at school but is somewhat irritable and contrary and possibly rather dull. Continues to take anti-epileptic medicine. Admitted to epileptic hospital at 16 years of age. Had been working in a coffee bar until admission. Convulsions had been very variable but usually only consisted of small jerks on the left side. Mental state: increasingly capricious and irritable. Physical examination: reduced power on the left side but no reflex changes. Appears psychologically normal though sensitive. E.E.G. repeated showed moderately severe dysrhythmia with spike-predominance on the left side.

Diagnosis: epilepsy, reduced power on the left side.

Summary: head injury at 6 months of age. Since 3 years of age left-sided convulsions. S.E.G. at 11 years of age ratio 0.32. Right-sided arteriography showed no definite abnormality. Operation over right hemisphere showed a small sunken area in the post-central region. At follow-up she was found to have been doing fairly well and had been able to work. Recently admitted to an epileptic hospital for medical treatment. Physical examination showed only slightly reduced power on the left side.

45.

N.K. no. 09683a/52. Boy born 16. 2. 45. No familial predisposition. First of two children. Pregnancy normal. Delivery prolonged but otherwise normal. Birth weight 3900 g.

Symptoms: injury to the back of the head at 3 years but no symptoms. From the age of 5 years slowly progressive uncertainty of movement, gait and speech difficulties, and difficulty with finer hand movements. Possibility of petit mal. Hearing uncertain. Examined in the R.H. Paediatric Department at 6 years of age. I.Q. 66. E.E.G.: no definite abnormality. L.E.G. unsuccessful on two occasions.

Admitted to N.K. department immediately afterwards. Head circumference 51.5 cm. Eye examination normal. Speech indistinct. Terminal tremor of finger movements most pronounced on right side. Gait broad-based and stiff. Right-sided Babinski.

V.E.G.: pressure 70. Ratio 0.32 (0.32/0.32). 3rd ventricle 8 mm. Temperature 38.6°C . the day following the examination. Otherwise no complications. On puncture the tissue appeared to be more resistant than normal.

Second admission to N.K. department at $7\frac{1}{2}$ years. Symptoms had progressed over the previous 10 months and particularly during the last 4. Was tired and disinterested in surroundings, could not walk or talk. Was not toilet-trained. Understood what was said

to him. Physical examination: E.E.G. probably abnormal. Skull X-ray normal. Eye examination normal. Made constant head movements and appeared to be very frightened. Bilateral Babinski.

V.E.G.: pressure 50. Clear fluid. Ratio 0.35 (0.35/0.35). 3rd ventricle 11 mm. Temperature 38.2° C. on the day of examination.

L.E.G.: two weeks later. Pressure 270. Clear fluid. Ratio 0.31 (0.31/0.31). 3rd ventricle? Temperature 37.9° C. Otherwise no complications.

Follow-up: was returned to the R.H. Neuromedical Department where he died shortly afterwards. No autopsy performed.

Diagnosis: possible leucoencephalopathy.

Summary: boy with protracted delivery who had a minor head injury at the age of 3 years. From the age of 5 years progressive gait and speech difficulties and tremor of the hands, possible petit mal. *V.E.G.* at the age of 6½ years showed a ratio of 0.32. Repeated *V.E.G.* at 7½ years showed a ratio of 0.35 and *L.E.G.* at the same time 0.31. He died shortly afterwards with a possible diagnosis of leucoencephalopathy.

46.

N.K. no. 08107/51. Girl born 17.9.44. No familial predisposition. Second of two children. Pregnancy and delivery uncomplicated. Birth weight 3000 g.

Symptoms: during the first year of life had a febrile disorder thought to be meningitis but without cerebral symptoms. Six weeks previous to admission at the age of 7 years had spontaneous status epilepticus. Admitted to a hospital for epileptics. Repeated E.E.G. showed activity corresponding to less than the age. *L.E.G.*: ratio 0.31 (0.31/0.31). 3rd ventricle 4 mm.

Admitted to N.K. department at 7 years of age. Head circumference 51 cm. Eye examination and X-ray of skull normal. E.E.G.: series of low frequencies, most pronounced over the right hemisphere. Severe focal dysrhythmia.

S.E.G.: pressure 200. Clear fluid. Ratio 0.32 (0.32/0.32). 3rd ventricle 5 mm. Normal distribution of surface air. No complications after examination.

Follow-up: has been well since discharge. Is in the grade according to age at a normal school. Physical examination: head circumference 53.5 cm. Eye examination normal. Reflexes brisk. Bilateral Chvostek reflexes and ankle clonus. Doubtful right-sided Babinski. Normal left-sided plantar response.

Diagnosis: healthy (abnormal reflexes).

Summary: girl who at one year of age had a febrile disorder, possibly meningitis. At the age of 7 years had spontaneous status epilepticus. *L.E.G.* ratio 0.31. *S.E.G.* 0.32. Since discharge has been perfectly well and attends a normal school. Has some abnormal reflex findings.

47.

N.K. no. 08207/51. Girl born 19.4.51. Familial predisposition: mother, father's mother and mother's mother have petit mal. Second of two children. Pregnancy: kicked in the lower abdomen in 6th and 9th month accompanied by vaginal bleeding and possible loosening of placenta. Delivery normal. Birth weight 3000 g.

Symptoms: at 2 months of age it was noticed in the nursery home that she was unusually rigid. Six weeks later she had ten brief episodes of tonic convulsions, upturned eyes, cyanosis and vomiting. Admitted to the R.H. Paediatric Department at the age of 5 months. Development normal. Increased muscle tonus. Bilateral Babinski. X-ray of skull normal. Eye examination and E.E.G. normal. Sub-dural puncture: on two occasions there were drops of blood in the fluid on the left side, no fluid on the right side.

Admitted to N.K. department at 6 months of age. Head circumference 41 cm. Eye examination normal. Smiled, focused, gripped and tried to stand. Brisk tendon reflexes and Babinski.

V.E.G.: pressure 150. Ratio 0.32 (0.33/0.30). 3rd ventricle 4 mm. Some cortical air, especially frontally. Temperature 38.3° C. the same day.

Follow-up: under out-patient supervision in a paediatric department and admitted several times when developmental quotient was found to be 80. E.E.G. slightly abnormal.

Intermittent squint present. Neurological examination normal. Is seizure-free and well.

Diagnosis: intellectual inferiority, previous epilepsy.

Summary: girl with familial predisposition for petit mal. Trauma occurred during pregnancy. Rigidity noticed at 2 months of age and was shortly after followed by brief convulsions. V.E.G. at 6 months showed a ratio of 0.32. 3rd ventricle 4 mm. At follow-up doing well without any seizures. Developmental quotient 80. Apart from intermittent squint no abnormality found.

48.

N.K. no. 08484/51. Boy born 3. 12. 51. No information on familial predisposition. Second of three children (twin A). Pregnancy normal. Birth weight 2350 g.

Symptoms: when 10 days old there was colour change and jerking spasms in arms and legs. He was listless after the attack. Admitted to a paediatric department where puncture through the fontanelles revealed slightly cloudy, bloodstained fluid on the right side which later cleared. On the left side there was cloudy, bloodstained fluid which did not clear. X-ray of skull normal.

Admitted to N.K. department at 3 weeks: healthy appearance. Eye examination normal. Head circumference 37 cm. Moves all four extremities. Reflexes normal. Subdural puncture normal. E.E.G. not done.

V.E.G.: clear fluid. Ratio 0.32 (0.33/0.30). 3rd ventricle 3 mm. Temperature 38.2° C. on the same day, otherwise no complications. Non-communicating septum cyst possibly present.

Follow-up: treated with phenemal for a short time. Physical and mental development completely normal. Walked at twelve months and talked at the normal time. At 4 months had concussion after falling off a cupboard. Was unconscious for half an hour and vomited. Admitted to hospital for ten days and made an uncomplicated recovery. Physical examination: normal, healthy appearance. Head circumference 55 cm. Eye examination normal. Normal reflexes. Harrison's sulcus and pes planus.

Diagnosis: healthy.

Summary: a boy, twin A, who had colour change and spasmodic jerks from the age of 10 days. V.E.G. at 3 weeks showed a ratio of 0.32, 3rd ventricle 3 mm. Has developed normally since the age of a few months and is now healthy.

49.

N.K. no. 22492/54. Boy born 2. 6. 54. No familial predisposition. Fourth of four children. Pregnancy and delivery normal. Birth weight 4250 g.

Symptoms: lay still the whole time and development appeared retarded. Generalised convulsions occurred at the age of 6 weeks and were accompanied by rigidity. He bent his head backwards, had a fixed stare, his legs and arms jerked and he had respiratory difficulties. Admitted to R.H. Paediatric Department at age of 3 months. Nystagmus present. E.E.G. severely abnormal with focus over left occipital region. Sub-dural puncture: no fluid on left side, clear fluid on right side.

Admitted to N.K. department at 3 months of age. Eye examination: possibly slight ptosis on the right side, otherwise no abnormality. Head circumference 44.5 cm. Lay still and did not react to examination. Bilateral Babinski.

V.E.G.: pressure 130, clear fluid. Ratio 0.32 (0.30/0.34). 3rd ventricle 3 mm. No rise in temperature or other complications.

Follow-up: own doctor reported that patient died at home of bronchopneumonia and emaciation the following year. No autopsy performed.

Diagnosis: oligophrenia, ? degree, epilepsy.

Summary: a boy who was retarded from birth and at 6 weeks of age had generalised convulsions. V.E.G. at 3 months showed a ratio of 0.32. 3rd ventricle 3 mm. He died at home at the age of one year from bronchopneumonia and emaciation.

50.

N.K. no. 22591/54. Girl born 14. 6. 46. Familial predisposition: mother had febrile convulsions as a child. First of three children. Pregnancy normal, delivery protracted. Birth weight 3750 g.

Symptoms: contracted measles at the age of 18 months and this was accompanied by convulsions of several hours' duration. No further symptoms until a month before admission when she complained of flickering before the eyes (had seen a pig killed). She became restless and muddled, and later had jerks in her arms. Admitted to a neuro-medical department. L.E.G. showed some asymmetry of the temporal horn, otherwise nothing abnormal.

Admitted to N.K. department at the age of 8 years 4 months. Eye examination normal. Head circumference 53 cm. X-ray of skull: large venous grooves. Calcification in falx cerebri. E.E.G: moderate to severe abnormality with many low frequencies, waves and spikes with left-sided predominance. Neurological examination: predominance of right patellar and Achilles tendon reflex. No Babinski.

S.E.G: pressure 450, clear fluid. Ratio 0.32 (0.31/0.32). 3rd ventricle 6 mm. Left temporal horn dilatation. Normal surface air. No complications following examination.

Follow-up: rather nervous but is doing well at school. Is seizure-free on phenytoin and attends a neurological department. E.E.G. has shown continued improvement but is nevertheless still abnormal with left-sided predominance. Physical examination: head circumference 54.3 cm. Eye examination and reflex examination normal. Motor system entirely normal. Plays piano well. Appears somewhat anxious but relaxes after a while and is then quite normal.

Diagnosis: healthy, previous epilepsy.

Summary: girl whose mother had febrile convulsions as a child. Birth was protracted. At 18 months of age had convulsions accompanying measles. At 8 years of age she complained of flickering before the eyes and later had jerks in the arms. S.E.G. at that time showed a ratio of 0.32. 3rd ventricle 6 mm. Apart from slight nervousness she appeared normal at follow-up. Is seizure-free on treatment. Is doing well at school.

51.

N.K. no. 1207/38. Girl born 15. 2. 25. No known familial predisposition. Normal delivery though possibly a little difficult. Otherwise no information on this period.

Symptoms: at age of 12½ years the patient fell off her bicycle and hit the right side of her forehead. Was only momentarily unconscious and not immediately put to bed. Had since had almost constant headache, worse on bending over. Became rather dizzy and tired after reading for a length of time but managed school work without difficulty.

Admitted to N.K. department at 13 years 4 months. Slightly tender over the right frontal and parietal regions. Eye examination and neurological examination normal. X-ray of skull normal.

V.E.G: pressure 150. Ratio 0.33 (0.30/0.35). 3rd ventricle 7 mm. (The pictures were measured from a copy in the case notes). Twenty-four hours after the examination the patient became listless. Lumbar puncture: pressure 490. Fluid slightly bloodstained. 22 ml. were withdrawn and the patient improved. She was transferred back to the R.H. Neuromedical Department where she had been admitted before the examination.

Follow-up: following her discharge from hospital she had many complaints, almost constant headache and a sharp increase in weight. She went back to school at the age of 13 years 7 months but for about a year her condition was worse than before V.E.G. She was treated with various tablets with some effect. Since the age of 20 has had almost constant unlocalised headache accompanied by nausea but never by vomiting. Has been married for eight years and worked in an office until four years ago. Feels extremely well apart from headache which she has got used to and which now bothers her less and less. Is periodically very nervous. Physical examination: head circumference 57 cm. Eye and neurological examination normal. Psychologically the patient appeared normal and well-balanced.

Diagnosis: post-concussional headache; sequelae of ventriculography.

Summary: a girl who at the age of 12½ years had a head injury followed by almost constant headache and dizziness. V.E.G. at 13 years showed a ratio of 0.33, 3rd ventricle 7 mm. Bloodstained cerebrospinal fluid found 24 hours after the examina-

tion. Headache has not varied very much over the years but recently has tended to improve. No other symptoms.

52.

N.K. no. 1637/39. Boy born 4.8.29. No familial predisposition. Only child. Pregnancy normal. Delivery four weeks premature. No asphyxia. Birth weight unknown.

Symptoms: 3 years earlier sustained a head injury with concussion and loss of consciousness for 5 minutes. In the 4 months before admission had attacks resembling petit mal at intervals of a few days to several weeks. On one occasion was found unconscious. In 5 weeks had two convulsions, the first left-sided which lasted 3 minutes, the other generalised. Admitted to R.H. Psychiatric Department when 10 years old. Transferred from there to R.H. Neuromedical Department.

Admitted to N.K. Department. Eye examination normal. There was paresis of the left-sided extensors of the arms. Reflexes: doubtful Babinski on the right, present on the left. Slight right-sided facial paresis. X-ray showed slight digital markings, mainly on the left side. E.E.G. not done.

V.E.G.: normal pressure. Ratio 0.33? (0.337/0.33). 3rd ventricle 4 mm. (Measurements taken from a copy of the pictures in the case records). Temperature 38.8° C. the same day; normal two days later.

Follow-up: the patient was admitted to a hospital for epileptics from the age of 14-15. The application for admission stated that he had been educated in a normal school for 7 years but that progress had been below average, and from the school's standpoint he was considered to be psychopathic with an I.Q. of at least 100. On admission a left-sided Babinski was found; neurological examination was otherwise normal. During his admission he did well and remained free of seizures. He was often insolent and unmanageable. During a cycling holiday he was found unconscious on a railway station and was admitted to hospital where a diagnosis of cryptogenic epilepsy was made. On examination he was slow to respond but neurological examination showed no abnormality. He was discharged the next day but re-admitted the same day with suspected barbiturate poisoning having been found unconscious in a garden with an empty bottle beside him from which at least 60 tablets had been taken during the preceding 24 hours. In spite of intensive treatment he died the following morning. Age at death was 18 years 10 months. Autopsy not carried out.

Diagnosis: epilepsy, psychopathy, barbiturate poisoning.

Summary: boy who at 7 years of age sustained a head injury and was unconscious. At 9½ he developed petit mal seizures, and later left-sided and generalised grand mal. V.E.G. at the age of 10 years showed a ratio of 0.33. At follow-up he had been admitted to a hospital for epileptics from the age of 14-15 years with psychopathic tendencies. Died from possible overdosage of phenobarbitone.

53.

N.K. no. 00199b/47. Boy born 28.12.34. No familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight normal.

Symptoms: between age of 1-2 years he fell several times and hit the back of his head. Was unconscious and had left-sided convulsions for about 30 minutes and a fracture was demonstrated in the right parietal region. Petit mal seizures occurred 6 months prior to admission.

First admission to N.K. department at 8 years 2 months. Physical examination revealed a 1.5 cm. depression. Eye examination normal. Appeared somewhat mentally retarded. X-ray of skull showed it to be large and thin-walled.

S.E.G.: pressure 200. Clear fluid. No ventricular air. No complications after the examination.

Second admission to N.K. department at 8 years 8 months. Constant petit mal and attacks of aphasia and left-sided facial paresis. E.E.G. showed severe dysrhythmia, particularly in the right hemisphere.

V.E.G.: ratio 0.33 (0.31/0.35). Third ventricle 5 mm. Temperature 38.4° C. on the same day with some headache. No complaints the next day.

Admitted to a hospital for epileptics at the age of 10 years where he continued to have convulsions. I.Q. 91.

Third admission to N.K. department at 12 years 7 months. Eye examination normal. E.E.G: generalised low frequencies.

S.E.G: pressure 110. Clear fluid. Pictures showed increased air over the convexity. No complaints after the examination.

Follow-up: admitted to a hospital for epileptics again at 13 years 2 months. E.E.G. unchanged. Repeat L.E.G: ratio 0.35 (0.33/0.39). 3rd ventricle 6 mm. During admission there were disciplinary difficulties. At 13 years 8 months he was found unconscious in the woods, deeply shocked and pulseless. On regaining consciousness after treatment with stimulants it emerged that he had fallen from a high tree. He died within a few hours.

Autopsy: there was a 16 cm. long tear in the liver with profuse bleeding (2 litres). Skull: no new injury but on the left side between the parietal and occipital areas there were signs of an old fracture. Over a 1.5 cm. area the bone was rather thin with a defect in the middle. Corresponding to this there was a fine adhesion to the brain surface though no actual scar. Cerebrum fairly normal and no new injury seen. No further examination performed.

Diagnosis: sequelae of fractured skull, epilepsy, psychological difficulties.

Summary: a boy who between the age of 1-2 years had a skull fracture in the right parietal region and developed petit mal. V.E.G. at that time showed a ratio of 0.33, 3rd ventricle 5 mm. Convulsions continued and repeated P.E.G.'s showed no change. He died at the age of 13 years 8 months after an accident while in a hospital for epileptics.

54.

N.K. no. 6473/45. Boy born 31.5.34. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3300 g.

Symptoms: normal development until possible head injury at the age of 3 years. He was found in clonic convulsions and investigated in the R.H. Neuromedical Department where a horizontal fracture in the occipital region with small fracture lines was found. Has since then had generalised convulsions accompanied by episodes resembling petit mal. During the year before admission there was increasing mental deterioration. He was slow, apathetic and forgetful and had behaviour difficulties. Admitted to R.H. Neuromedical Department.

Admitted to N.K. department at age of 11 years. Physical examination: appeared somewhat retarded. Eye and reflex examination normal. E.E.G: low frequencies, a few typical epileptic changes.

S.E.G: pressure 180, clear fluid. Ratio 0.33 (0.35/0.31). 3rd ventricle 7 mm. Normal surface air. Temperature 38.3° C. the day after examination, normal on third day.

Follow-up: admitted to epileptic hospital for 6 months at age of 14 years and again two years later. In a special home for epileptics from the age of 20. Had attended an exam-free school. I.Q. at age of 14 was 66. Only rare convulsions now. Repeated E.E.G. showed fairly severe dysrhythmia. L.E.G. at 14 years of age showed a ratio of 0.32/0.32. 3rd ventricle? L.E.G. at 17 years showed a ratio of 0.33/0.34. 3rd ventricle 6 mm. Cranial walls appeared somewhat thick. Physical examination: no motor difficulties. Head circumference 55 cm. There is unsustained bilateral ankle clonus. Reflexes otherwise normal. Speech good. Eye examination normal. Appears somewhat mentally retarded.

Diagnosis: debilitas mentis, epilepsy.

Summary: cranial fracture at 3 years of age after possible head injury followed by clonic convulsions, and later intellectual deterioration. P.E.G. at 11 years of age showed a ratio of 0.33. Under epileptic care since discharge and only has occasional convulsions. Repeated P.E.G.'s show no change. On physical examination he appeared normal apart from some reduction in mental ability.

55.

N.K. no. 7388/45. Girl born 19.12.42. Familial predisposition: mother had two generalised convulsions at the age of 15 and 16 after head injuries. First of two children. Pregnancy normal. Delivery 3 weeks premature, otherwise uncomplicated. Birth weight 2250 g.

Symptoms: when about 3½ years old sustained head injury followed by vomiting, pallor and sleep for a couple of hours. Three months later had a Jacksonian type of convulsion which began in the morning with vomiting and jerks on the left side. Admitted to a paediatric department. X-ray of skull showed calcification in the right parietal region (possibly old haematoma).

Admitted to N.K. department at 3 years of age. Eye examination normal. Doubtful bilateral Babinski. Psychological development corresponded to age. X-ray of skull: increased digital markings, deep posterior fossa. E.E.G. not done.

V.E.G.: pressure 200. Ratio 0.33 (0.33/0.33). 3rd ventricle 3 mm. Normal surface air. Right posterior horn more dilated than left. Temperature 38.2° C. the same day, normal the next day. No other complications.

Follow-up: during the year following examination had only occasional seizures with long free intervals. Thereafter seizure-free for about 6 years. Treatment discontinued at this time. When she was 14 years old again had an occasional seizure and treatment was resumed. E.E.G. performed 3 months later showed improvement compared with just before commencement of treatment. Physical examination: completely normal, healthy appearance. Head circumference 55 cm. Reflexes: ankle clonus on the left side and tendon reflexes slightly increased in the legs. Mentally completely normal. Doing well at school and has no motor difficulties.

Diagnosis: epilepsy (only rare seizures), otherwise healthy.

Summary: a girl whose mother had two generalised convulsions at the age of 15 and 16. Head injury at the age of 3½ years followed 3 months later by a Jacksonian type convulsion. V.E.G. showed a ratio of 0.33. 3rd ventricle 3 mm. Only occasional seizures following discharge and completely free for long intervals. Does well at school. Physical examination normal apart from slight reflex abnormalities.

56.

N.K. no. 0583/47. Boy born 9. 11. 46. No familial predisposition. Third of three children. Pregnancy normal. Delivery lasted 12 hours but was normal. Birth weight 4750 g.

Symptoms: since the age of 8 months attacks resembling petit mal with fixed and distant gaze. 2½ months previous to admission the patient had fallen out of his pram and attacks gradually increased. Admitted to hospital at 10 months of age. Treated with phenobarbitone.

Admitted to N.K. department at 11 months of age. Healthy appearance. Eye examination normal. Head circumference 45 cm. with "cracked pot" sound on percussion. Appeared frightened and restless. Reflexes normal. Mental development corresponded to age. X-ray of skull normal. E.E.G. not done.

S.E.G.: pressure 270. Ratio 0.33 (0.33/0.33). 3rd ventricle 5 mm. No complaints after examination.

Follow-up: immediately after discharge patient was seizure-free but when a year old he had another seizure and medicine was increased. When 6 years old he had been seizure-free for a couple of years but in the last half-year there had been increasing petit mal attacks again. After a further increase in dosage was once more seizure-free. In recent years minor seizures of 2-4 seconds' duration. I.Q. about 80, possibly a little higher. Attends a private school and does very well at arithmetic. Is emotionally somewhat unstable. Motor ability particularly good. Complains now and then of headache, especially in the morning. Physical examination: healthy, normal appearance. Intermittent convergent squint on right side. Head circumference 54 cm. Mental development probably corresponds to age.

Diagnosis: epilepsy, intellectual inferiority.

Summary: a boy who at age of 8 months developed petit mal seizures which increased after a fall at the age of 8½ months. S.E.G. at that time showed a ratio of 0.33. At follow-up there had been seizure-free periods and at present the seizures are well-controlled. I.Q. is approximately 80.

57.

N.K. no. 06065b/50. Boy born 13.7.41. Familial predisposition: mother had fainting spells but no convulsions. First of two children. Pregnancy and delivery normal. Birth weight normal.

Symptoms: ptosis of right upper eyelid present since birth. Otherwise no symptoms in neonatal period or infancy. From the age of 13 months to 3 years had 4 attacks of loss of consciousness and clonic convulsions on the right side. Thereafter seizure-free for a couple of years, and then 4-5 seizures in 18 months. Admitted to epileptic hospital at the age of 6 and 6½ years.

L.E.G.: ratio 0.33 (0.34/0.32). 3rd ventricle 6 mm. Moderate amount of surface air especially frontally but probably not pathological. E.E.G. showed slight dysrhythmia.

First admitted to N.K. department when nearly 7 years old unconscious with clonic convulsions on both sides of the face, most pronounced on the right side. In addition had clonic convulsions in the right arm and leg. Physical examination showed right-sided ptosis and convergent squint. Apart from slightly reduced function of right facial nerve no neurological abnormality found. E.E.G. showed dysrhythmia with low frequencies over left occipital region. Left-sided arteriography showed no real abnormality.

Operation performed on the left side of the cranium. The dura was normal and below it was a collection of fluid. Moderate diffuse microgyri present. A 2 × 3 cm. area downwards towards the limit between the occipital and frontal lobes seemed a little sunken. No localised processes. No complications following operation.

Second admission at 8 years 8 months and third admission 5 months later due to convulsions. On both occasions appeared to be in status epilepticus. Other than E.E.G. no examinations carried out.

Follow-up: admitted to epileptic hospital after first admission to N.K. department. Has since been under out-patient supervision partly at epileptic hospital and partly in R.H. Neuromedical Department. Has had some attacks resembling petit mal and once in connection with fever had an attack of grand mal. Has a number of minor psychiatric difficulties at home. Is a messenger in a bank and likes the work. Physical examination: normal, healthy appearance. Ptosis of right upper eyelid. Brisk reaction of left facial nerve. Tendon reflexes brisk but presumably not pathological. External examination of the cranium revealed a well-healed scar on the left side. Head circumference 56 cm. Mental development: appeared to be rather clinging and unsure, but otherwise normal for his age.

Diagnosis: epilepsy, slight psychogenic difficulties associated with puberty, ptosis of right upper eyelid.

Summary: boy who had ptosis since birth and from the age of 13 months episodes of unconsciousness and right-sided convulsions. L.E.G. at the age of 6 years showed a ratio of 0.33. Operation on the left side showed a moderately diffuse microgyri with an area under surface level. At follow-up there had been a few petit mal seizures and a single grand mal seizure. He is now working as a messenger and except for some puberty difficulties appears to be normal.

58.

N.K. no. 02201/48. Girl born 28.1.44. Familial predisposition: diabetes and epilepsy in the family. Mother has two cousins who are feeble-minded. Father committed suicide at 40. Third of three children. (The two eldest were stillborn and both were 4 weeks premature). Pregnancy normal. Delivery induced two months before time. Breech presentation and forceps delivery. Asphyxia present. Bilateral clavicular fractures and signs of intracranial bleeding immediately after birth. Birth weight 3400 g.

Symptoms: flaccid and apathetic from the beginning. Operation for removal of dermoid cyst on neck performed at 4 months of age. Since the age of 2 years episodes of right-sided Jacksonian seizures. When 4½ years old patient could neither walk nor stand alone. Crawled with the help of the arms. Said single words. Was not toilet trained and could not feed herself.

Admitted to N.K. department at 4 years 7 months. Appeared oligophrenic and did not co-operate. Eye examination normal. Could focus and smile. Spastic paraplegia in legs

most pronounced on the left side. Slight spasticity in left arm. Doubtful Babinski. X-ray of skull: protrusion of right side.

V.E.G: pressure 60, clear fluid. Ratio 0.33 (0.32/0.34). 3rd ventricle 4 mm. Increased cortical air. Temperature 38.2° C. on third day, otherwise no complaints.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department for two years. Operated on at the age of 5 years for elongation of the Achilles' tendon and transposition of the hamstrings. Admitted to a State mental institution at the age of 6½. Developmental quotient 47. E.E.G. at age of 8 years: focus in the left frontal region. Transferred to another State institution at the age of 9 years with a diagnosis of imbecility, spastic tetraplegia and possible epilepsy. Developmental quotient 33. During admission was given physiotherapy and made good progress. Talks well and feeds herself. Is always happy and smiling. Understands what is said to her and enjoys playing. Physical examination: large, pleasant child. Puberty starting. Appears much more intelligent than her I.Q. of 33 would indicate. Severe spastic tetraplegia with subluxation of left hip. Cannot walk without support. Head circumference 50 cm. Eye examination normal. Speech good.

Diagnosis: oligophrenia (? imbecility, ? idiocy), spastic tetraplegia, previous epilepsy.

Summary: girl with diabetes, epilepsy and mental retardation in the family. Forceps delivery because of breech presentation. There were signs of intracranial bleeding immediately after birth. From the age of 2 years had right-sided Jacksonian seizures. Mental and motor development retarded. V.E.G. at 4 years of age showed a ratio of 0.33, 3rd ventricle 4 mm. Later a number of orthopaedic operations were carried out. Placed in a State mental institution at the age of 6 years. I.Q. 33. Spastic tetraplegia and subluxation of the left hip present.

59.

N.K. no. 08151/51. Girl born 23.4.51. Familial predisposition: father's sister is somewhat retarded. Third of three children. Pregnancy and delivery normal. Birth weight 4200 g.

Symptoms: at the age of one week it was noticed that the patient was spastic. Shortly afterwards seizures occurred accompanied by cyanosis, opisthotonus and trembling of all extremities. Occurred up to six times each day. Admitted to hospital at the age of 4 months. In opisthotonus position the whole time with the legs crossed. Later the seizures were characterised by the arms being turned to the left. Admitted to the R.H. Paediatric Department at about 5 months of age. E.E.G. was abnormal with spike foci over the entire right hemisphere. Sub-dural puncture: yellowish, bloodstained fluid on the right side; no fluid on the left side. Retarded both physically and mentally.

Admitted to N.K. department at the age of 6 months. Eye examination normal. Head circumference 41 cm. Pronounced back stiffness. Could not focus. Moderate hypertonicity of legs with very brisk patellar reflexes. No Babinski. X-ray of skull normal. Sub-dural puncture revealed no abnormality. V.E.G. was unsuccessful.

S.E.G: pressure 300. Ratio 0.33 (0.32/0.34). 3rd ventricle 8 mm. Rather a large collection of surface air present particularly in the Sylvian fissure area. After V.E.G. was attempted there was oedema of the entire right side of the skull. No complications following S.E.G.

Follow-up: transferred from R.H. Paediatric Department to another hospital where patient remained until her death some six weeks later at the age of 9 months. There had been a steady increase in the number of seizures and they lasted several hours. She was completely disinterested in her surroundings and was very miserable. Physical examination: in opisthotonus position the whole time. Arms and legs rigid and no reflex responses could be elicited. X-ray of skull normal. During admission temperature rose to 40.5° C. and later at short intervals to 39.8° C. During the 24 hours immediately preceding her death the temperature rose from 38° C. to 40.7° C. Autopsy was not performed.

Diagnosis: spastic tetraplegia, epilepsy, oligophrenia.

Summary: a girl whose father's sister was somewhat retarded. At one week of age she was noticed to be spastic and shortly afterwards seizures occurred. S.E.G. at 6 months showed a ratio of 0.33. Large collection of cortical air present. Transferred to an-

other hospital where she stayed until her death 6 weeks later after a period of increasing convulsions and rigidity.

60.

N.K. no. 20804/53. Girl born 9.9.41. No familial predisposition. Pregnancy and birth normal. Birth weight 2600 g. Left-sided harelip.

Symptoms: after severe whooping-cough at the age of 8 years periodic headache localised to the left side of the forehead. This was accompanied by epigastric pain, nausea and vomiting. On two occasions when she was 11 years old she fainted for a few seconds without any accompanying convulsion. She also had transitory speech difficulties. When she was 12 years old she had a sudden reduction of power in the right leg followed by a similar condition in the right arm and down the left side of the face lasting altogether half an hour and followed by headache over the left side of the forehead. School attendance normal.

Admitted to N.K. department at 11 years 9 months. Eye examination and reflexes normal. X-ray of skull: increased digital markings, no abnormality. E.E.G. showed increased activity of low frequency. Spikes, sharp waves and square waves mostly over the left hemisphere parieto-temporally. Bilateral arteriography showed well-filled vessels in normal position.

S.E.G.: pressure 200, clear fluid. Ratio 0.33 (0.32/0.35). 3rd ventricle 6 mm. Surface air normally distributed. Temperature 39° C. the day after, normal four days later.

Follow-up: E.E.G. at the age of 14 years slightly abnormal. Seizure-free since admission and discontinued medicine a year ago. Headache not particularly troublesome. Did well at school and left at normal age. Now helps at home. Physical examination: normal, healthy appearance. Head circumference 56.5 cm. Eye examination normal. Reflexes in arms brisk. Patellar reflexes normal. No Babinski. No ankle clonus. Speech and mental state completely normal.

Diagnosis: healthy.

Summary: a girl who was born with a left-sided harelip developed left-sided headache after whooping-cough at 8 years of age. At the age of 11 years had transitory reduction of power in the right arm and leg. S.E.G. ratio 0.33. 3rd ventricle 6 mm. At follow-up there had been no seizures since admission and medicine had been discontinued. She appeared to be completely well.

61.

N.K. no. 20833/53. Boy born 14.1.44. No familial predisposition. Second of three children. Pregnancy was complicated by bleeding during the ninth month. Delivery normal. Birth weight 3750 g.

Symptoms: otitis media at 9 months. Infantile epidemic gastroenteritis at the age of a year. After this intestinal disorder he could neither stand nor talk and development was very slow. Investigated in the R.H. Child Psychiatric Department at the age of 7 years where his developmental quotient was found to be 51. Always complained of headache localised to the right and frontally. No seizures. E.E.G. at the age of 8 years showed severe dysrhythmia bilaterally, most pronounced to the right and frontally.

Admitted to N.K. department at the age of 9 years 5 months. Eye and reflex examination normal. Appeared oligophrenic. X-ray of skull normal. E.E.G. severely abnormal. Low-frequency activity on both sides.

S.E.G.: pressure 300. Ratio 0.33 (0.31/0.36). 3rd ventricle 5 mm. No surface air. No complications following the examination.

Follow-up: is under State mental care at home and has attended a special school since the age of 10 years. A variety of tests have indicated a severe degree of mental retardation. On physical examination reflexes were normal. Head circumference 55 cm. Motor ability good. Speech almost understandable. Mental development appears to correspond to 7 years.

Diagnosis: oligophrenia (? debilitas mentis, ? imbecility).

Summary: a boy who after acute gastroenteritis at one year of age slowed down in development and at the age of 7 years developmental quotient was 51. He complained

of frequent headaches and S.E.G. at that time showed a ratio of 0.33. 3rd ventricle 5 mm. Is now under State mental care at home.

62.

N.K. no. 20888/53. Girl born 4. 1. 52. No familial predisposition. Only child. Pregnancy and delivery normal. Patient very flaccid. Birth weight 4375 g.

Symptoms: during admission to hospital at the age of 5 months on account of nasal catarrh, the family's attention was drawn to the fact that the child's head was very small. After that it was remarked that the patient was physically retarded. Could not sit up at the age of nearly 18 months. Legs and arms were spastic and jerked every now and then. Admitted to a neurosurgical department and later to R.H. Paediatric Department. E.E.G. showed severe dysrhythmia. X-ray of skull normal.

Admitted to N.K. department when nearly 18 months old. Smiled but appeared severely mentally retarded. Head circumference 42 cm. Eye examination: alternating convergent squint. Considerable spasticity of all extremities. Tendon reflexes brisk. Bilateral Babinski.

S.E.G.: pressure 180, clear fluid. Ratio 0.33 (0.35/0.31). 3rd ventricle 8 mm. Increased air present over the right hemisphere, especially frontally. Temperature 38.4° C. the day after examination, otherwise no complications.

Follow-up: investigated many times as an out-patient in the R.H. Paediatric Department. Frequent left-sided jerks. Head circumference at the age of 2 years 10 months was 43.5 cm. Constant rigidity and adductor spasms. Under State mental care at home from the age of 3-4 years. Died 14 days before admission to a State institution had been arranged. On enquiry at the home, it was said that the child enjoyed company, laughed and chattered. The legs were rather stiff and could not be straightened. She was not toilet trained. No autopsy performed.

Diagnosis: oligophrenia (idiotcy), spastic tetraplegia, microcephaly, epilepsy.

Summary: a girl who was slightly flaccid at birth and was found at 5 months of age to have a small head and to be very retarded. S.E.G. when nearly 18 months old showed a ratio of 0.33 and increased cortical air. 3rd ventricle 8 mm. The head did not increase in size over the following years and rigidity continued. She died just before admission to a State mental institution.

63.

N.K. no. 3680/42. Boy born 18. 4. 36. No known familial predisposition. Seventh of seven children. Pregnancy complicated by vomiting. Delivery lasted 9 hours. The patient was slightly asphyxiated and had a haematoma on the neck. Birth weight unknown.

Symptoms: at about 6 months of age convulsion chiefly affecting the left side. Thought to be due to infantile tetany. Squint during the early years. At the age of 2 years the patient had a generalised clonic convulsion. After convulsions at 6 years of age and again 6 weeks before admission left-sided hemiplegia occurred. Vomiting often accompanied the convulsions.

Admitted to N.K. department at the age of 6½ years. Mental ability appeared to correspond to age. The left shoulder could not be raised. Eye and reflex examination normal. X-ray of skull showed it to be large with thin walls and parasagittal vein-like markings. E.E.G. not done.

V.E.G.: ratio 0.34 (0.33/0.34). 3rd ventricle 8 mm. Temperature 38.4° C. the same day, normal on the second day. Otherwise no complications.

Follow-up: patient had spent most of his childhood in an epileptic hospital. At the age of 7 he was in status epilepticus. Since the age of 17 he has been under epileptic care, partly in a special home and partly under family care. During this time he was thought to be almost psychopathic. I.Q. assessed at the age of 15 was 55. L.E.G. performed at the age of 17 showed a ratio of 0.39 (0.42/0.35). 3rd ventricle 9 mm. Right side - 7 mm. E.E.G. has been severely abnormal most of the time and there have been daily episodes of petit mal. Is on anti-epileptic treatment. Is mentally dull but physically normal. Speech is normal.

Diagnosis: epilepsy, oligophrenia (debilitas mentis).

Summary: a boy who was slightly asphyxiated at birth. Convulsions affecting the left side occurred at 6 months of age and later became generalised. V.E.G. at 6 years of age showed a ratio of 0.34. 3rd ventricle 8 mm. Has since been under epileptic care. I.Q. at 15 years was 55. Behaviour is psychopathic.

64.

N.K. no. 9477a/47. Boy born 29. 4. 36. Familial predisposition: mother and brother appear dull. In addition many members of the family have psychopathic tendencies and intellectual inferiority. Second of three children. Pregnancy and birth normal. Birth weight unknown.

Symptoms: always somewhat retarded, wild and unmanageable. At the age of 10 had an uncharacteristic (? seizure) episode without a previous injury. Admitted to a psychiatric department where E.E.G. showed dysrhythmia. I.Q. was 77. Convulsion occurred 3 months later.

Admitted to N.K. department at that time.

V.E.G.: pressure 60. Ratio 0.34 (0.34/0.33). 3rd ventricle? The picture showed a typical septum pellucidum cyst. Temperature 38.4° C. on the same day.

Re-admitted to N.K. department at the age of 11 years. Eye examination normal. Bilateral Babinski. E.E.G. showed moderate dysrhythmia, most pronounced posteriorly and to the right. X-ray of skull normal. Right-sided arteriography showed no abnormality.

S.E.G.: pressure 240, clear fluid. The cyst had disappeared. Ratio 0.34 (0.35/0.34). 3rd ventricle 4 mm. Temperature 38.2° C. on the same day. Otherwise no complications.

Follow-up: admitted to an epileptic hospital at 11 years of age, and since the age of 17 has been in a special epileptic home. Very seldom has seizures. L.E.G.: (at 15 years of age) showed a ratio of 0.37 (0.36/0.38). 3rd ventricle not measurable. L.E.G.: (at 18 years of age) showed a ratio of 0.37 (0.36/0.38). 3rd ventricle not clearly outlined. Physical examination: well-developed, tall and strong. Physically normal. Mentally appeared somewhat retarded. Head circumference 56 cm. Reflex examination normal apart from a doubtful left-sided ankle clonus. Finger-nose and finger-finger test normal. Romberg negative. Eye examination normal.

Diagnosis: epilepsy, intellectual inferiority.

Summary: a boy in whose family several members show intellectual inferiority and psychopathic tendencies. Had a convulsion at the age of 10 years. V.E.G. ratio then was 0.34 and the picture showed a septum pellucidum cyst. Repeated P.E.G.'s over the following years showed that the cyst had disappeared but otherwise the findings were unchanged. He is in a home for chronic epileptics and appears slightly mentally retarded.

65.

N.K. no. 8559/46. Girl born 25. 2. 42. No familial predisposition. First of two children. Pregnancy normal. Delivery normal except for 3 weeks' prematurity. Birth weight 2250 g.

Symptoms: fell out of a bunk-bed the day before admission but had no immediate symptoms. Later became ill, began to smack her lips and lost consciousness. Was still unconscious on admission to hospital and on transfer.

Admitted to N.K. department at the age of 4½ years. Unconscious with left-sided convulsions and trismus. Bilateral Babinski. Eye examination showed slight blurring of the discs nasally, presumably physiological. X-ray of skull normal. Cisternal puncture: pressure 130, fluid bloodstained, presumably due to puncture. Improved over the following 24 hours and on examination 3 days after the only abnormality was a right-sided Babinski. E.E.G. showed diffuse dysrhythmia.

S.E.G.: pressure 150, clear fluid. Ratio 0.34 (0.34/0.34). 3rd ventricle 8 mm. No rise in temperature or other complications.

Follow-up: became free from convulsions after a year but continued anti-epileptic treatment for a further year. Is doing well at school. No headache or other symptoms. Physical examination: normal, healthy appearance. Head circumference 53 cm. Speech and mental development completely normal. Eye and reflex examination also normal.

Diagnosis: healthy.

Summary: a girl who at the age of 4½ years fell from a bunk-bed without any

immediate symptoms but later became unconscious and had left-sided convulsions. S.E.G. ratio 0.34. 3rd ventricle 8 mm. The seizures continued for a year but have now ceased. She is completely fit and has no symptoms at all.

66.

N.K. no. 0245/47. Girl born 18. 2. 39. No familial predisposition. Fourth of four children. Pregnancy normal. Delivery rather protracted. Birth weight 3500 g.

Symptoms: at the age of a year injured the back of her head without loss of consciousness or vomiting. At the age of 3 years convulsions began and have been increasing in frequency. Admitted to R.H. Paediatric Department for a short time and then to the N.K. department at the age of 8½ years. Eye examination: slight hypermetropia. E.E.G.: moderate dysrhythmia. X-ray of skull showed increased digital markings.

V.E.G.: pressure 50, clear fluid. Ratio 0.34 (0.34/0.34). 3rd ventricle 4 mm. Normal distribution of cortical air. Temperature 38.6° C. the day after the examination.

Follow-up: family doctor wrote from Iceland to say that the patient died at the age of 9½. She had been taking medicine regularly and a few days before her death became sick so the medicine was stopped. She was active until a few hours before she died but just before was severely shocked. The family doctor was convinced that it was a case of drug intoxication accompanied by intracranial haemorrhage. No autopsy was performed.

Diagnosis: epilepsy.

Summary: a girl who injured the back of her head at the age of a year without immediate symptoms. Had an increasing number of convulsions from the age of 3 years. V.E.G. at 8½ years showed a ratio of 0.34, 3rd ventricle 4 mm. Was under regular medical treatment, presumably became intoxicated by the drug and died from a possible intracranial haemorrhage.

67.

N.K. no. 01032/48. Boy born 6. 11. 39. No familial predisposition. Pregnancy normal. Delivery protracted, 3 days. Admitted to hospital for medical induction. Patient was asphyxiated at birth. Birth weight 3750 g.

Symptoms: at the age of 5½ years had a generalised convulsion without any apparent reason, followed by a similar episode a year later. At the age of 8 years, two months before admission, jerks occurred down the right side. Admitted to the R.H. Neuromedical Department at the age of 9 years. E.E.G. revealed severe dysrhythmia with occasional epileptic changes on the left side.

Admitted to N.K. department at 9 years of age. Physical examination: large head circumference. Bilateral Babinski. Eye examination and skull X-ray normal. E.E.G. slightly abnormal.

V.E.G.: pressure 60. Ratio 0.34 (0.35/0.32). 3rd ventricle? Normal surface air. No complications.

Follow-up: at the age of 12 years had a severe convulsion. None noticed since and has been without treatment for the past 3–4 years. Did well at school and left at the age of 15 years. Works in a factory and also does farm work. Symptom-free apart from slight headache. Physical examination: head circumference 58 cm. Eyes, mental state, speech and motor system all normal. Reflexes: the only abnormality is a doubtful right-sided ankle clonus. Inclines to the right when walking because of slight scoliosis of the thoracic spine.

Diagnosis: previous epilepsy, thoracic scoliosis.

Summary: boy who was asphyxiated at birth and had a generalised convulsion at 5½ and again at 6½. At the age of 8 years right-sided jerks occurred. V.E.G. showed a ratio of 0.34, 3rd ventricle? Last had a seizure at the age of 12 years and is now off anti-epileptic medicine. Has a job and except for a slight scoliosis physical examination is entirely normal.

68.

N.K. no. 01585/48. Boy born 4. 2. 48. No familial predisposition. Only child. Pregnancy complicated by pain in the fourth month. Delivery at normal time but accelerated by injections. Lasted 4½ hours. Birth weight 3000 g.

Symptoms: was blue for the first 24 hours of life. At about the age of a month had spasmodic twitches especially around the eyes. Cried a lot and was very restless. At the age of 5-6 weeks there were jerks in the arms and some time after generalised convulsions with loss of consciousness for about 10-20 minutes. Admitted to the R.H. Paediatric Department. A varying degree of rigidity of the extremities present and occasional jerks, particularly in the left arm. Sub-dural puncture and skull X-ray normal.

Admitted to N.K. department when a little more than two months old. Head circumference 38 cm. Eye examination normal. Sub-dural puncture revealed clear fluid on both sides.

V.E.G.: the ventricular system appeared somewhat dilated but in the normal position. The pictures were rather unclear but a degree of dilatation could be seen. Ratio 0.34, side measurement uncertain. 3rd ventricle 3 mm. No complications following the examination.

Follow-up: about a week after discharge was admitted to another neurosurgical department. Repeated P.E.G. showed a ratio of 0.36 (0.29/0.42). 3rd ventricle not measurable. At about 4 months of age operation was performed over the right hemisphere. The gyri in the temporal region were widened and pale. Towards the Sylvian fissure there were two cysts under a very thin rim of cortical tissue. Along the Sylvian fissure and the central fissure there was increased sub-arachnoid fluid. After removal of 3 cm. of cortical tissue in the pre-motor region an area was reached resembling tumour tissue in that it was grey and tough and in some places gelatinous with small fluid-filled cavities. After removal of an area the size of half a hen's egg the operation was discontinued as normal tissue could not be reached. Microscopy of the cortex showed it to be underdeveloped with pronounced gliosis. The sub-cortical tissue showed degeneration with atrophy and oedema. No real tumour tissue. It was thought to be a so-called "malformation tumour". Seizures continued post-operatively. The patient was transferred to a paediatric department. He was very rigid with a pronounced tendency to opisthotonus and cerebral crying. He developed a febrile disorder considered to be meningitis, became increasingly rigid and died at 6 months of age. No autopsy performed.

Diagnosis: epilepsy, rigidity, congenital cerebral dysplasia.

Summary: a boy who was somewhat cyanotic in the first 24 hours. At one month of age he developed jerks and later on generalised convulsions and rigidity. V.E.G. at two months of age showed a ratio of 0.34, 3rd ventricle 3 mm. Repeated V.E.G.'s revealed cortical dysplasia with fluid-filled cavities. The rigidity increased, he developed a febrile disorder and died at 6 months of age.

69.

N.K. no. 02083/48. Girl born 25. 2. 46. No familial predisposition. Third of three children. Pregnancy: hypertension and albuminuria. Birth normal. Birth weight 3500 g.

Symptoms: vaccinated against diphtheria at the age of 2 years 2 months and febrile for a few days afterwards. She then developed twitching round the right eye and in the right arm. Increasing seizures, bilateral and clonic with momentary loss of consciousness. Admitted to hospital. Seizures increased during admission, lasted up to two minutes and occurred as many as 35 times a day. Admitted to R.H. Neuromedical Department at the age of 2 years 4 months and diagnosed as a case of sequelae of acute encephalitis, post-vaccination in origin. The seizures decreased to five daily on phenobarbitone. Eye examination, skull X-ray and lumbar puncture normal.

Admitted to N.K. department at 2 years 5 months. Eye examination normal. Appeared rather flaccid and fat. Reflexes normal. Had repeated seizures beginning as tonic convulsions in the right arm, loss of consciousness for a few seconds, followed by right-sided and later left-sided myoclonic jerks. E.E.G. not done.

S.E.G.: pressure 350. Ratio 0.34 (0.32/0.35). 3rd ventricle 10 mm. Temperature 38° C. the same day, otherwise no complaints.

Follow-up: continued to have seizures for 5 months after discharge and was then seizure-free for the next 4 years. Following smallpox vaccination, however, seizures recurred and she was admitted to hospital because of petit mal. E.E.G. showed moderate

diffuse dysrhythmia. Since then there have been minor seizures only and at long intervals. Admitted to hospital at the age of 10 years 4 months and medicine discontinued. Is doing well at school. Physical examination: patient is small and rather fat but does not appear to have any endocrine disorder. Head circumference 56.2 cm. Eye examination normal. Reflexes normal apart from bilateral Babinski. No ankle clonus. She walks, runs, stands and jumps completely normally.

Diagnosis: epilepsy (petit mal), very rare seizures, otherwise healthy.

Summary: a girl who developed localised jerks after diphtheria vaccination. S.E.G. ratio 0.34, 3rd ventricle 10 mm. Seizures gradually ceased during the next few years but returned after smallpox vaccination. No real seizures since the age of 10 years. Physical examination normal except for bilateral Babinski.

70.

N.K. no. 03118/49. Boy born 19. 2. 37. No familial predisposition. First of three children. Pregnancy normal. Birth two months premature; possible asphyxiation. Birth weight 1250 g.

Symptoms: in addition to possible asphyxiation he sustained a head injury as the mid-wife dropped him and he hit his head on the bottom of the bath. Reduced power of the left side of the body was present until he was 3 years old but has since not been noticed. Has never been able to hear and at the age of 7 years he went to a deaf and dumb school where he learnt to talk and did well. When a little more than 11 years he had repeated episodes of nausea, gyratory dizziness, vomiting and frequent nystagmus. Admitted several times to hospital.

Admitted to N.K. department at the age of 12 years. Left-handed. Eye examination normal. Otological examination: left-sided acoustic neuro-labyrinthopathy and total right-sided deafness. X-ray of skull showed the walls to be thin, and the posterior fossa deep. There were numerous increased digital markings. Slight nystagmus on extreme lateral eye movements. E.E.G: many diffuse abnormal findings.

V.E.G: pressure 100, clear fluid. Ratio 0.34 (0.34/0.34). 3rd ventricle not measureable. Temperature 39.4°C . the same day. Slight neck stiffness and dizziness for several days. Normal temperature on the fourth day after penicillin.

Follow-up: He attended the deaf and dumb school and development was entirely normal. There were no seizures. He now attends a coaching school and is working for exams. Plays badminton, dances etc. Speech is completely normal. Occasionally uses a hearing-aid. Has no physical defects. The doctor at the State institution for the deaf reported that the patient had been there until the age of 18 and had no physical handicap. The diagnosis was one of left-sided partial deafness and right-sided total deafness.

Diagnosis: reduced hearing, otherwise healthy.

Summary: a boy who was born 2 months prematurely and presumably asphyxiated sustained a head injury immediately after birth. Always had hearing difficulties. At the age of 11, episodes of nausea, vomiting and dizziness. V.E.G. at the age of 12 showed a ratio of 0.34, 3rd ventricle not measureable. He is now doing very well, is sitting for examinations and has no abnormal physical finding except for the decreased hearing.

71.

N.K. no. 03802/49. Boy born 16. 5. 40. No familial predisposition. First of two children. Pregnancy normal. Birth two weeks premature. Labour lasted 2-3 days. Did not breathe for 15 minutes. Birth weight 2400 g.

Symptoms: poor weight gain and jaundice for the first month of life. No tendency to opisthotonus. Was very restless for the first 12 months and thereafter developed normally. When one year old developed a right-sided squint (later operated on at the age of 7 years). Walked at 18 months and talked at the normal time. Did well at school. Balance always poor. At about the age of 4 years after a slightly febrile episode in connection with a cold he fainted. Subsequent episodes occurred at intervals of 2 weeks to 2 months. He complained of impaired vision, seemed withdrawn for about 5 minutes, became unconscious and flaccid. Two months prior to admission had a generalised convulsion lasting 10 minutes.

Admitted to N.K. department at the age of 9 years. Sequelae of operation for right

convergent squint. Gait unsteady and head and arms moved in continuous small jerks. Tendon reflexes brisk. No Babinski. Skull X-ray showed increased digital markings, otherwise nothing abnormal. E.E.G: abnormal with an occasional epileptic formation on the right side, especially occipitally.

S.E.G: pressure 250, ratio 0.34 (0.36/0.32). 3rd ventricle 3 mm. Temperature 39.2°C . the day after otherwise no complaints.

Follow-up: manages school with some difficulty. Hearing decreased. A hearing-aid was suggested but there were no real difficulties at home and the family did not think it necessary. Continues to have convulsions but they are decreasing and now occur only every 6 months. Works as a grocer's errand-boy and is attending a trade school. Is rather clumsy but does not lack strength. Physical examination: right convergent squint. Speech is poor and sounds as though he does not open his mouth enough. Uses his hands normally. Reflexes in the arms brisk and those in the legs not definitely abnormal. Mentally rather slow but not really retarded. E.E.G. at the age of 16 years showed moderate to severe abnormality.

Diagnosis: epilepsy, dysarthria.

Summary: a boy who did not breathe for the first 15 minutes and who was jaundiced for the first month of life. Had always had gait difficulties and when 4 years old had episodes of fainting followed by seizures. S.E.G. ratio 0.34, 3rd ventricle 3 mm. Seizures decreased. He has some hearing difficulties but manages his work and on examination only minor abnormalities were found.

72.

N.K. no. 03913/49. Boy born 1.8.46. Familial predisposition: maternal uncle had convulsions as a child. First of two children. Pregnancy normal. Delivery difficult and about 2 weeks premature. Lasted $2\frac{1}{2}$ days. There was secondary arrest of labour. The child was not asphyxiated. Birth weight 2850 g.

Symptoms: admitted to a paediatric department at the age of 3 weeks because of otitis and meningitis. Since then retarded in development. Began to walk at 2 years but gait unsteady. Appeared to be feeble-minded. In recent months, at the age of about 3 years, attempts to talk have been accompanied by choreatic movements of the left hand.

Admitted to N.K. department at the age of 3 years. Oligophrenic and impossible to make contact with. Eye examination showed possible atrophy of the optic nerve. Head circumference 46 cm. Reflexes not definitely abnormal. X-ray of skull: deep posterior fossa, otherwise no abnormality.

S.E.G: pressure 250. Ratio 0.34 (0.32/0.35). 3rd ventricle 17 mm. Respiration ceased after the examination but was re-established after stimulant injections. No rise in temperature and only slight sleepiness the next day.

Operation was performed on the left side to explore the possibility of a sub-dural haematoma. The dura looked bluish and translucent. It became apparent that the left temporal lobe had become one large cyst and communication had been established between the inferior horn and the cyst. Microscopy: the cyst wall showed a traumatic brain lesion with old haemorrhage. Temperature following operation was 38.5°C . He collapsed during the evening and his blood pressure fell. He recovered after stimulant injections. Apart from this episode there were no post-operative complications.

Follow-up: admitted to a State mental institution at the age of 4 years 3 months. Diagnosis was idiocy and operation performed for a cyst of the left temporal lobe. Head circumference on admission was 45 cm. Over the next year or two it was noticed that he was running around without difficulty. There was no intellectual improvement, he was neither dry nor clean, and he had to be helped with everything. Physical development was fairly good. Physical examination: head circumference 45.9 cm. Large and clumsy with a fat, expressionless face. Does not talk and dribbles a great deal. Walks and runs without difficulty. Uses his hands fairly well. No squint and no neurological changes.

Diagnosis: oligophrenia (idiocy).

Summary: a boy with a family history of convulsions and a difficult birth. Developed

otitis and meningitis at the age of 3 weeks and development then slowed down. S.E.G. ratio 0.34, 3rd ventricle 17 mm. Operation showed a large cyst in the left temporal lobe with communication with the ventricular system. He is in a State mental institution and is making no intellectual progress.

73.

N.K. no. 04918/50. Boy born 6. 8. 39. No information on familial predisposition. Second of two children. Birth precipitate. No asphyxia but he cried poorly to start with and was flaccid. Birth weight 3250 g. No jaundice but general condition was poor.

Symptoms: at the age of two months had a convulsion following administration of castor oil. Had always been mentally and physically backward. Walked at 4 years, not toilet trained until 10 years. At the age of 18 months was admitted to the R.H. Paediatric Department and at 5 years Stoffel's operation and elongation of Achilles tendon performed. Did not go to school.

Admitted to N.K. department at the age of 10 years 7 months. Appeared rather retarded. Left-handed. Eye examination: right pupil larger than left. Expressive aphasia present. Power in right arm reduced and the legs appeared rather spastic. Right-sided Babinski and ankle clonus. X-ray of skull normal. E.E.G: moderate dysrhythmia, chiefly occipitally and on the right side.

S.E.G: pressure 0, clear fluid. Ratio 0.34 (0.33/0.36). 3rd ventricle 6 mm. No increase of surface air. Temperature 37.7° C. the same day, otherwise no complications.

Follow-up: is under State mental care at home. Was briefly admitted to a State institution for observation at the age of 12 years. Investigated at the Orthopaedic Hospital's cerebral palsy clinic at the age of 15 years and moderate spasticity found. The result of the earlier operations must be said to be good. Repeated I.Q. assessments at the age of 12, 15 and 16 approximately 30. Mother says improvement continues. Physical examination: has difficulties with movement especially going up and down stairs. Talks badly, laughs uncontrollably. Is very fat and heavy. There is spastic tetraplegia with more pronounced involvement of the legs than the arms. Operation scars present. Abduction of hips less than 90°. Tendon reflexes very brisk. Head circumference 54 cm. Eye examination normal.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, obesity.

Summary: a boy whose delivery was precipitate and who had a convulsion at the age of two months. Always retarded in development. Various operations performed for spastic tetraplegia. No school attendance. S.E.G. ratio 0.34, 3rd ventricle 6 mm. Is under State mental care at home. I.Q. approximately 30. Has a spastic tetraplegia mainly involving the legs.

74.

N.K. no. 05553/50. Girl born 14. 11 48. No familial predisposition. Third of three children. Pregnancy normal. Birth 3 weeks premature. Birth weight 2500 g.

Symptoms: almost immediately after birth had spells of crying and a tendency to opisthotonus. Poor general condition and frequent vomiting. Mental and physical development retarded. Admitted to a paediatric department because of extreme loss of weight and frequent episodes of fever. E.E.G. showed no definite abnormality.

Admitted to N.K. department at 18 months of age. Examination showed her to be flaccid and on the defensive. All four extremities spastic. Reflexes difficult to assess. Head circumference 46 cm. Eye examination normal. Skull X-ray showed coarse, scattered digital markings. Thin cranial bones, principally over the posterior sinus. Bilateral burr holes showed no sign of hygroma.

S.E.G: pressure 450, clear fluid. Ratio 0.34 (0.31/0.36). 3rd ventricle 4 mm. There was increased surface air corresponding to right Sylvian fissure and insular area. Temperature after examination 39° C. and after S.E.G. 38.4° C.

Follow-up: was admitted to a paediatric department at the age of 3 years and was examined at the Orthopaedic Hospital's cerebral palsy clinic at the age of 5 and on two further occasions. She has a severe spastic tetraplegia with complicating contractures. Microcephaly is also present, the head circumference being 48.5 cm. at the age of 8

years. She is very small and though development is difficult to assess, function is definitely retarded. There is severe dysarthria.

Diagnosis: spastic tetraplegia with contractures, oligophrenia (? degree), microcephaly, dysarthria.

Summary: a girl who since birth had crying spells and a tendency to opisthotonus. Poor mental and physical development. Burr holes at the age of 18 months showed no sign of hygroma. S.E.G. ratio 0.34, 3rd ventricle 4 mm. Increased surface air in the area of the right Sylvian fissure and insular area. At follow-up she had a severe spastic tetraplegia and function was extremely retarded.

75.

N.K. no. 06423/50. Boy born 23. 4. 47. No familial predisposition. Only child. Pregnancy and birth normal. Birth weight 3500 g.

Symptoms: 3 episodes of right-sided convulsions accompanied by loss of consciousness during the last 3 months, the last one an hour in duration. Headache on a couple of occasions but otherwise lively and intelligent. Admitted to a paediatric department at the age of 3½ years. X-ray of skull and eye examination normal. E.E.G: severe dysrhythmia with focus over the left hemisphere.

Admitted to N.K. department at the age of 3½ years. Eye and neurological examinations normal. Skull X-ray normal.

V.E.G: pressure 90, clear fluid. Ratio 0.34 (0.34/0.34). 3rd ventricle 2 mm. No complaints after the examination.

Left-sided arteriography showed no abnormality.

Operation over the left hemisphere: the cortex appeared normal. Parasagittally in the post-central region there were some microgyri with diffuse collection of fluid. Posterior to the centre of the temporal lobe was a sunken area measuring 2×2 cm. and electrocortico-graphy pointed to a focus here. The area was coagulated. Maximum temperature was 39° C. Otherwise no complications.

Follow-up: apart from a few seizures in the post-operative period he has been seizure-free since but has occasional headache. Takes phenobarbitone in small doses. Is doing well at school and is physically normal. E.E.G. at the age of 6 years slightly abnormal but considerably less so than previously. The focal changes have disappeared. Physical examination: head circumference 55.2 cm. Eye and neurological examination normal.

Diagnosis: healthy, previous epilepsy.

Summary: in 3 months had 3 right-sided convulsions for no known reason. V.E.G. ratio 0.34, 3rd ventricle 2 mm. Left-sided operation showed in the middle of the temporal lobe a small sunken area which was coagulated. At follow-up seizure-free apart from a few seizures post-operatively. Is on small doses of medicine and doing well at school. Physical examination entirely normal.

76.

N.K. no. 06565/50. Girl born 7. 10. 45. No familial predisposition. First of two children. Pregnancy normal. Forceps delivery and no respiration for an unknown length of time. Birth weight 3100 g.

Symptoms: always very retarded, both physically and mentally. Investigated in the R.H. Paediatric Department at the age of 2 years and admitted to a State mental institution at the age of 4 years. During admission two seizures which were not precipitated by fever.

Admitted to N.K. department at the age of 5 years. Impossible to make contact with the child. She could not walk. Eye examination showed myopia and convergent squint. Reflexes normal. X-ray of skull: brachycephalic skull with deep posterior fossa. E.E.G: no definite abnormality.

V.E.G: pressure 180. Ratio 0.34 (0.33/0.35), 3rd ventricle 6 mm. No excess of surface air. Temperature 38° C. the same day, normal on the third day. No complications.

Follow-up: patient was transferred from one State institution to another at the age of 7 years. Developmental quotient corresponded to less than 3 years. Needs help with every-

thing, cannot talk and does not understand what is said to her. Made no progress during her stay. Had occasional episodes of petit mal but no grand mal. Physical examination: head circumference 52 cm. Eyes: slight squint, otherwise normal. Reflexes brisk with extended zones. Unsustained ankle clonus. Doubtful bilateral Babinski.

Diagnosis: oligophrenia (idiocy), epilepsy.

Summary: girl delivered by forceps and without respiration for an unknown length of time. Always retarded mentally and physically. Had two convulsions at the age of 4 years. V.E.G. ratio 0.34, 3rd ventricle 6 mm. Placed in a State mental institution. Has occasional petit mal attacks and has made no progress whatsoever.

77.

N.K. no. 07707/51. Boy born 14. 11. 46. Familial predisposition: mother had convulsions at the age of 2 years after whooping-cough. Second of two children. Pregnancy normal. Birth difficult and patient was blue. Birth weight 3500 g.

Symptoms: at the age of 3 he had prolonged right-sided otitis media. At the age of 4 he had 4-5 generalised convulsions which started on the left side. Admitted to a paediatric department. E.E.G. normal.

Admitted to N.K. department at 4 years 8 months. Eye examination and neurological examination normal. E.E.G.: severe focal dysrhythmia localised to the left fronto-temporal and central regions.

S.E.G.: pressure 300, clear fluid. Ratio 0.34 (0.34/0.34). 3rd ventricle 3 mm. Temperature 38.6° C. the day after, otherwise no complications.

Follow-up: had a few convulsions after discharge but has since been seizure-free and during the past year medicine has been discontinued. Has an occasional headache and attends special reading classes. Physically normal and examination revealed no neurological abnormality. Eyes normal. Head circumference 55 cm.

Diagnosis: headache, previous epilepsy.

Summary: a boy whose mother had convulsions. Delivery was difficult. At 3 years of age had otitis and at 4 years convulsions occurred. S.E.G. ratio 0.34, 3rd ventricle 3 mm. At follow-up except for occasional seizures shortly after discharge had been completely seizure-free and off medicine for the past year. Attends a special reading class.

78.

N.K. no. 07955/51. Girl born 4. 12. 50. No familial predisposition. Fourth of four children. Pregnancy: pains in the 9th month. Delivery prolonged. Membranes ruptured 12 hours before. Injections given. Birth weight 3850 g.

Symptoms: flaccid and sleepy after birth. Would not suck. At 10 days of age had generalised convulsions with opisthotonus lasting 3 hours. Admitted to R.H. Paediatric Department. Convulsions continued. Lumbar and sub-dural puncture normal. E.E.G.: severe focal dysrhythmia, mainly localised to the right hemisphere in the temporal region.

Admitted to N.K. department at 9 months of age. Appeared severely mentally retarded. Did not react to sound. Eyes: convergent squint. Head circumference 45 cm. Muscle tone difficult to judge but child appeared very stiff when the upright position was assumed. Tendon reflexes brisk. Bilateral Babinski. X-ray of skull normal.

V.E.G.: pressure 70, clear fluid. Ratio 0.34 (0.35/0.34). 3rd ventricle 6 mm. Temperature 39.4° C. the day after, normal next day.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Patient had many episodes of fever of unknown origin at home. Admitted to a State mental institution at the age of 5 years and died 3 days later. The day after admission her temperature rose sharply and she became muddled and withdrawn. It appeared that a cerebral factor was the most likely as there was no real infection. She was given antibiotics but the temperature rose steadily to 42° C. During the last 24 hours there was constant twitching of the face and extremities. No neck stiffness. No autopsy performed.

Diagnosis: oligophrenia (idiocy), epilepsy, hyperpyrexia of presumed cerebral origin.

Summary: a girl whose delivery was of long duration and who was flaccid after birth. Generalised convulsions at 10 days which steadily increased. V.E.G. ratio 0.34, 3rd ven-

tricle 6 mm. Admitted to State mental institution where she died 3 days after admission in presumed cerebral hyperpyrexia.

79.

N.K. no. 08082/51. Girl born 18. 12. 50. No familial predisposition. Only child. Pregnancy normal. Delivery about a month premature and precipitate. Child was severely cyanosed and had to have stimulants. Birth weight 3000 g.

Symptoms: in poor general condition since birth. Two days after delivery almost black and lungs said to be collapsed. Admitted to hospital. Head grew rapidly after birth. She could not sit upright at the age of 9 months and was re-admitted to hospital.

Transferred to N.K. department at the age of 10 months. Eye examination normal. Head circumference 48 cm. "Cracked pot" sound on cranial percussion. Fontanelles bulging. Could focus but could not hold head up. X-ray of skull: rather large, thin-walled with deep posterior fossa. Sub-dural puncture showed no hygroma.

V.E.G.: pressure 50, clear fluid. Ratio 0.34 (0.32/0.36). 3rd ventricle 4 mm. Temperature 38.4° C. the day after. Some days later burr holes performed on both sides. A possible slight increase in sub-arachnoid fluid but normal otherwise.

Follow-up: walked at 2 years and 4 months and talked at the normal time. Had occasional attacks of tonsillitis with fever but no cerebral complications. At the age of 6 years was examined by a doctor from a State mental institution who reported astounding progress since brain operation. On intelligence tests she was not mentally retarded but only borderline and in consequence could not be taken into State mental care. Motor development normal. No seizures. Speech rather lisping. Physical examination: head circumference 55.9 cm. (All members of the family have large heads). Reflexes normal. Movements free and hand movements particularly good.

Diagnosis: macrocephaly (? familial), ? intellectual inferiority.

Summary: girl whose birth was precipitate and who was severely cyanosed. Because of retarded motor development and a large head V.E.G. was performed at 10 months of age. Ratio 0.34, 3rd ventricle 4 mm. At follow up she had made astounding progress mentally and was only borderline. Except for a possible familial macrocephaly nothing abnormal could be found.

80.

N.K. no. 08959/52. Boy born 26. 8. 51. No familial predisposition. Third of three children. Pregnancy and delivery normal. Birth weight 3700 g.

Symptoms: generalised clonic convulsions at the age of 4 months which ceased on administration of phenobarbitone. Patient appeared mentally dull and did not know his parents. Admitted to R.H. Paediatric Department at the age of 5 months. Skull X-ray normal. Eye examination normal. E.E.G. normal at first, but on later examination there were spike-waves localised to the right parieto-occipital region.

Admitted to N.K. department at the age of 7 months. Eye examination showed right-sided optic nerve atrophy and possibly the same condition on the left. Could not focus and did not smile. There were constant movements of all extremities. Bilateral Babinski.

V.E.G.: ratio 0.34 (0.36/0.32). 3rd ventricle? No rise in temperature or other complications after the examination.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Is under State mental care at home. Has had no seizures since the age of a year. E.E.G. at the age of 3 years showed no definite abnormality. Physical examination: looks very well. Walks and stands normally. Is happy and contented and never exposes himself to danger. During a lengthy visit he trotted around contentedly but did not touch anything. Appears to get on very well with his brothers and sisters. Watches his fingers a great deal. Physical development would appear to be normal. Head circumference 52 cm. Reflexes normal.

Diagnosis: oligophrenia (imbecility).

Summary: boy who at 4 months of age developed generalised clonic convulsions and seemed to be mentally retarded. V.E.G. ratio 0.34, 3rd ventricle? Is an imbecile and under State mental care at home.

81.

N.K. no. 21778/54. Girl born 14. 8. 44. Familial predisposition: third child was born with hydrocephalus and myelomeningocele and died at birth. Patient is the fourth of seven children. Pregnancy and delivery normal. Birth weight 3300 g.

Symptoms: serious head injury at the age of 3 years when she was struck on the right side of the head with a telephone pole and was unconscious for 3 weeks. The accident was followed by an immediate spastic paralysis of the left leg. Admitted to hospital for almost two months and paralysis gradually decreased. At the age of 7 years complained of headache. At age of 9 years had a convulsion in the morning accompanied by jerks down the left side. After this the left arm was paralysed. A further episode occurred a month later and thereafter the seizures increased in frequency until they were occurring up to 4 times a day. Had 15 such seizures altogether. Admitted to R.H. Neuromedical Department. E.E.G. showed severe focal abnormality with spikes and waves, activity of low frequency in the right occipital region.

L.E.G.: ratio 0.34 (0.34/0.34). 3rd ventricle 9 mm. There was a bone defect corresponding to the right parieto-occipital region. Temperature 38° C. the same day but no other complaints.

Admitted to N.K. department at the age of 9 years 9 months. Eye examination revealed hypermetropia. Head circumference 54 cm. Slight left-sided spastic hemiparesis with Babinski and brisk tendon reflexes. Slight dysaesthesia in the left arm. Mental development normal.

Operation performed over the posterior part of the right hemisphere. Dura opened around the lesion which was an 8 cm. long meningo-cerebral scar. Electrocorticography showed spikes downwards temporally and frontally. Post-central gyrus was only affected in the lower and posterior part. The right trigonum was widely opened to remove the glia tissue around the scar. Laterally and upwards there was a completely free cyst containing xanthochrome fluid. Slight temperature after operation but otherwise no complications. Microscopy showed meningo-cerebral scar.

Follow-up: followed up as an out-patient in N.K. department. Is doing well and manages school work without difficulty. There is only slightly decreased power in the left arm. Fields of vision normal. E.E.G. practically unchanged. There have been no convulsions since the operation except on a single occasion when medication was omitted. Is somewhat bothered by left-sided hemiplegia but can do handwork. Gets tired easily but has no real complaints. Menstruation has begun. Physical examination: healthy, normal appearance. Mental state normal. Head circumference 56.5 cm. No squint. Positive ankle clonus on both sides and left-sided Babinski. Patellar reflexes normal. Tendon reflexes very brisk in the arms, particularly on the left. Finds it difficult to perform quick movements with the left hand. Finger-nose test poor on the left side.

Diagnosis: left-sided spastic hemiplegia, epilepsy.

Summary: girl whose older sibling had hydrocephalus and myelomeningocele and died at birth. At 3 years of age she had a severe head injury and was unconscious for 3 weeks. From the age of 9 years had left-sided convulsions. L.E.G. ratio 0.34. 3rd ventricle 9 mm. Operation revealed an 8 cm. meningo-cerebral scar over the right hemisphere as well as a cyst. At follow-up there had been no seizures. Left-sided spastic hemiplegia continues. Mental development normal.

82.

N.K. no. 22218/54. Girl born 27. 1. 54. Familial predisposition: father had convulsions at the age of 5-6 years. Only child. Pregnancy normal. Birth medically induced. Asphyxia lasted one hour. About half the placenta was calcified. Birth weight 3100 g.

Symptoms: admitted to hospital immediately because of signs of cerebral damage. She was restless, trembling, on the defensive and making spasmodic jerking movements. Re-admitted at the age of two months with tonic convulsions in the legs. Last admission because of tendency to opisthotonus at the age of 4 months. E.E.G. showed generalised dysrhythmia. X-ray of skull normal.

Admitted to N.K. department at the age of 4 months. Eye examination normal. Head

circumference 41 cm. Hyperactive reflexes and bilateral Babinski. X-ray of skull normal. E.E.G. definitely abnormal with spike focus in the right fronto-temporal region. Sub-dural puncture normal.

L.E.G.: pressure 300, clear fluid. Ratio 0.34 (0.33/0.36). 3rd ventricle 7 mm. Even distribution of surface air. Temperature 37.8° C. the same day, otherwise no complications.

Follow-up: admitted to a hospital for epileptics at the age of 7 months until her death two months later. Had numerous attacks of petit mal and grand mal. Was febrile for several days during the month before her death and at the time of her death she had a high temperature which had not responded to treatment. Cause of death pneumonia. No autopsy performed.

Diagnosis: epilepsy, oligophrenia (? degree), incipient spastic tetraplegia.

Summary: girl whose father had convulsions as a child. Birth was precipitate and she was asphyxiated for an hour. The placenta was partly calcified. Since birth there had been increasing signs of intracranial damage with seizures. *L.E.G.* at the age of 4 months showed a ratio of 0.34, 3rd ventricle 7 mm. Admitted to a hospital for epileptics where she had continuous convulsions and died at the age of 9 months from pneumonia.

83.

N.K. no. 24231a/56. Boy born 8. 3. 54. No information available on familial predisposition or pregnancy. Delivery difficult, face presentation. Placenta delayed. Birth weight 4100 g.

Symptoms: was cyanotic for the first week of life. Admitted to hospital at the age of a month because of a fracture of the left arm. Generalised spasms at the age of 2 months. Admitted to the R.H. Neuromedical Department at the age of 5 months because of seizures. E.E.G. severely abnormal. Mental development retarded.

Admitted to N.K. department at 6 months. Eye examination normal. Could smile and focus. X-ray of skull normal.

V.E.G.: all air on the surface. Repeat *V.E.G.*: pressure 150, clear fluid. Ratio 0.34 (0.32/0.35). 3rd ventricle 8 mm. Temperature 38.6° C. the day after.

Follow-up: has continued to have seizures particularly on effort. Re-admitted to hospital at the age of 22 months. E.E.G. showed an abnormal curve, particularly localised to the right hemisphere. *V.E.G.*: ratio 0.32 (0.28/0.36). Right side - 5 mm. 3rd ventricle 4 mm. No complications after the examination apart from a temperature of 39.2° C. the same day. Since discharge the patient has been seen as an out-patient on several occasions. Convulsions continue. The family doctor has recently written to say that the patient is very active. In spite of anti-epileptic drugs he is frequently troubled by seizures but these can be controlled by rectal chloral.

Diagnosis: epilepsy.

Summary: boy who had a difficult delivery and who was cyanotic for the first weeks of life. Generalised convulsions occurred at the age of 2 months. *V.E.G.* ratio 0.34, 3rd ventricle 8 mm. Because of continued convulsions *V.E.G.* repeated, ratio 0.32. Is still having convulsions but is otherwise well.

84.

N.K. no. 24155a/56. Boy born 24. 12. 54. No familial predisposition. First of two children. Second child died at the age of 15 months from congenital brain damage. Autopsy showed aplasia of the left cerebral hemisphere. Pregnancy: pain in the lumbar region extending down the legs during the last 3-4 months of pregnancy. Delivery 4 weeks premature and difficult. Brow presentation. No asphyxia. There were pressure marks and a haematoma in the left temporal region. Birth weight 3630 g.

Symptoms: at about the age of a month he had numerous episodes of opisthotonus lasting about 3 minutes. Admitted to hospital at the age of 5 months. Diagnosed as a case of cerebral palsy and imbecility.

Admitted to N.K. department at the age of 6 months. Eye examination normal. Head circumference 41.5 cm. Variable degree of rigidity present. Tendon reflexes in the legs

brisk. X-ray of skull showed no definite abnormality. E.E.G: possible abnormality in the left hemisphere with predominance of depressed and low activity.

V.E.G: pressure 100, clear fluid, later bloodstained. Cortex appeared normal. The pictures were not very satisfactory. The ratio could not be definitely assessed as one obtained the impression that the ventricles were partially fused but it was probably 0.34, 3rd ventricle 7 mm. Temperature 38° C. the day after. No other complaints.

S.E.G: two days later. Pressure 300, clear fluid. There was obvious communication with a large air collection over the left hemisphere. Ratio 0.34 (0.33/0.34). 3rd ventricle 10 mm. No complications.

Operation performed over the middle part of the left hemisphere. The previously seen porencephaly was shown to be a defect in the upper half of the hemisphere. There was a clear pia cyst with ingrowth of the vessels. The defect was opened just in front of the motor region. The septum pellucidum was partially destroyed so that one could see into the lateral ventricle on the other side. Microgyri were present downwards but gyri appeared almost normal otherwise. Biopsy showed cortex with artificial changes. Fibrosed leptomeninges. Temperature 39° C. the day after operation and normal on the fifth day. No further complications. Small collection of fluid under the operation flap.

Follow-up: has been fairly well since admission. No seizures. Possibly has slight difficulty in seeing things approaching from the left. Likes to crawl but cannot walk or sit. Physical examination: spastic tetraplegia. Head circumference 44.7 cm. Re-admitted at the age of a year with a view to reconsideration of therapeutic procedures. S.E.G: pressure 650. Ratio 0.34 (0.35/0.33). 3rd ventricle 10 mm. One had the impression that the cavity did not lead to the surface but that there was a more limited cyst in connection with the system. E.E.G. showed no abnormality. Was somewhat upset after the examination with a temperature of 39.4° C. but this had fallen to normal on the third day. Has since shown some improvement both physically and mentally. Understands a lot of what is said and has no seizures. Can walk in a walking-chair but cannot sit unsupported. Reflex changes such as those seen in spastic tetraplegia are present. Head circumference at the age of 3 years 46.8 cm. No hyperkinesis. I.Q. presumably about 40-50.

Diagnosis: oligophrenia (? imbecility), spastic tetraplegia.

Summary: a boy whose younger brother had aplasia of the left hemisphere. Backache during pregnancy and delivery difficult. Because of repeated attacks of opisthotonus V.E.G. was performed at the age of 6 months. This showed a communication between the ventricular system and an air collection in the left hemisphere. Ratio 0.34, 3rd ventricle 7 mm. Operation revealed a defect in the left hemisphere. At follow-up had made some progress. I.Q. is assessed at between 40 and 50 and spastic tetraplegia is present.

85.

N.K. no. 3427/42. Boy born 23. 10. 38. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 4400 g.

Symptoms: at the age of 2 years had a convulsion and was found unconscious in the farmyard. Convulsions increased particularly during the 6 months prior to admission. Admitted to hospital because of concussion following a convulsion. There had been disturbance of speech during the previous six months so that it had become completely impossible to understand him. For 4-5 months there had been intermittent paresis of the back and extremities.

Admitted to N.K. department at the age of 3 years 9 months. Eye examination normal. Development less than according to age and said only single words. Neurological examination normal.

V.E.G: ratio 0.35 (0.34/0.36). 3rd ventricle 7 mm. Temperature 38.8° C. the same day, normal on the third day. No other complications.

Follow-up: admitted to hospital, last time at the age of 14 years. Diagnosed as whooping-cough, intellectual inferiority and epilepsy. Appeared retarded. There were atypical plantar reflex responses on the right side. Various examinations including eye examination and skull X-ray were normal. Had had no seizures since admission to the N.K.

Department. Own doctor wrote that at the age of 18 years the patient was completely fit and able-bodied and was working as a farmer.

Diagnosis: possible intellectual inferiority, otherwise healthy.

Summary: a boy who at two years of age had a convulsion and over a period of 6 months at the age of 3 years developed increasing convulsions, speech difficulties and intermittent paresis of the extremities. V.E.G. at 3 years 9 months showed a ratio of 0.35 3rd ventricle 7 mm. At follow-up he was said to be somewhat retarded but otherwise completely fit.

86.

N.K. no. 20446a/53. Girl born 3.7.41. Familial predisposition: alcoholism, epilepsy and nervous disorders in the family. Second of three children. Pregnancy normal. Delivery two weeks premature. Cord around the neck. Patient was asphyxiated for an hour. Birth weight unknown.

Symptoms: since the first month of life had a left-sided convergent squint. Began to talk at the age of 3 years and was thought to be intellectually normal. Three weeks before admission had increasing right-sided convulsions with subsequent right-sided hemiparesis. Admitted to a paediatric department at the age of 3 years 9 months. Convulsion beginning as tonic, later clonic spasms on the right side accompanied by loss of consciousness. X-ray of skull showed no definite abnormality. Eye examination normal.

Admitted to N.K. department at the age of 3 years 9 months. Eyes: hypermetropia and left-sided convergent squint. Presumably somewhat retarded. Gait unsteady and ataxic. No definite paresis. Used right hand very little. X-ray of skull: possibly increased intracranial pressure. E.E.G. not done.

V.E.G.: pressure 240. Ratio 0.35 (0.35/0.35). 3rd ventricle 5 mm. Temperature 40.1° C. the day after, normal on the 7th day. Otherwise no complications.

Re-admitted to N.K. department at the age of 11½ with continuous focal seizures localised to the right side and occasional attacks of petit mal. I.Q. at that time 63. Eye examination: hypermetropia and convergent squint. Slight left-sided equinus deformity. X-ray of skull normal. E.E.G. severely abnormal with spike formation.

Follow-up: under State mental care at home from the age of 8-9 years. I.Q. at the age of 8 years 57, and at 9 years 75. Attended a special school and did well. Discharged from mental care at the father's wish. Admitted at the age of 11 years to the R.H. Paediatric Department and L.E.G. showed a ratio of 0.40 (0.38/0.42). 3rd ventricle 7 mm. Admitted to an epileptic hospital from the age of 13-14 years and her mental ability found to be somewhat reduced. There was pronounced kyphoscoliosis convex to the left. L.E.G. at the age of 13 years showed a ratio of 0.44 (0.38/0.49). 3rd ventricle 11 mm. Admitted to a home for chronic epileptics where she has remained since. Is doing fairly well but has a few difficulties at school. Still has occasional seizures resembling those previously described together with attacks of petit mal.

Diagnosis: intellectual inferiority, epilepsy.

Summary: girl with a familial predisposition to neuro-psychiatric disorders. The cord was round the neck and she was asphyxiated for one hour. At the age of 3½ had right-sided seizures and right-sided hemiparesis. V.E.G. ratio 0.35, 3rd ventricle 5 mm. L.E.G. at 11 years showed a ratio of 0.40 and at 13 years 0.44. 3rd ventricle 11 mm. Continues to have focal seizures and attacks of petit mal and is now in a home for chronic epileptics.

87.

N.K. no. 7203/45. Boy born 13. 6. 32. Familial predisposition: brother paranoid. Fourth of four children. Pregnancy and delivery normal. Birth weight over 3000 g.

Symptoms: during the 5-6 years prior to admission had periodic headache over the eyes. Might have followed slight head injury. During the year immediately before admission had episodic headache which began after a definite head injury without loss of consciousness. Precipitated by noise and could last most of the day. Did well at school but became increasingly bad-tempered and irritable.

Admitted to N.K. department at the age of 13 years 4 months. Eye and neurological

examination normal. X-ray of skull showed possible intracranial calcification. I.Q. 96. E.E.G. not done.

S.E.G.: pressure 120. Ratio 0.35 (0.35/0.35). 3rd ventricle 3 mm. Temperature 37.7° C. the day after examination. No other complications.

Follow-up: completely well since discharge and has only occasional headache. Did well at school and left at the age of 15 years. Completed his Army service and has had different jobs since. Sustained a head injury at the age of 22 without apparent ill-effect. Physical examination: head circumference 56.5 cm. Eye and neurological examination normal.

Diagnosis: healthy.

Summary: a boy who from the age of 8 years had periodic headaches after a possible minor head injury. At the age of 12 years became increasingly bad-tempered and irritable. *S.E.G.* at the age of 13 $\frac{1}{4}$ showed a ratio of 0.35, 3rd ventricle 3 mm. At follow-up he had done his military service and had had several different jobs. Was completely fit.

88.

N.K. no. 21321/53. Boy born 8.3.44. Familial predisposition: mental disease and nervousness in family. Second of three children. Pregnancy: no information. Delivery normal. Birth weight unknown.

Symptoms: always very restless. At the age of 6 years had measles and was delirious for 48 hours. Besides behaviour difficulties had "always" had poor muscle co-ordination. Admitted to a children's convalescent home at the age of 9 years. I.Q. approximately 100.

Admitted to N.K. department at the age of 9 years. Left-handed. Somewhat restless and tiresome. Eye examination: divergent squint. Poor coordination but no real ataxia. Doubtful left-sided Babinski. Other examinations normal. X-ray of skull normal. Head circumference 55 cm. E.E.G. moderately abnormal. Increased number of low frequencies, particularly over the right occipital region.

S.E.G.: pressure 180, clear fluid. Ratio 0.35 (0.35/0.35). 3rd ventricle 5 mm. Normal distribution of cortical air. Temperature 39.2° C. the day after the examination, normal on the 4th day. Otherwise no complaints.

Follow-up: because of difficulties at home, particularly maternal over-care, the patient has been in a children's home since the age of 10 years. Has had to change schools because of disagreements with the teacher. I.Q. at age of 10 years 125-130. Never has convulsions. Physical examination: healthy, normal appearance. Head circumference 55 cm. Eye examination normal. Reflexes in arms brisk. Patellar reflexes could be elicited over a wide area. No Babinski, no ankle or patellar clonus. Feet in excavatus position, such as seen in Friedreich's ataxia. Finger-nose test uncertain, finger-finger test good. Romberg negative. No difficulty with quick movements. No balancing difficulties.

Diagnosis: bad environmental influence, otherwise well.

Summary: boy with family history of mental illness and nervous disorders. Always said to be nervous and this increased after a severe attack of measles. *S.E.G.* at 9 years of age showed a ratio of 0.35, 3rd ventricle 5 mm. At follow-up found to be of high intelligence and apart from behaviour difficulties due to bad environmental influence there was no abnormality.

89.

N.K. no 22277/54. Boy born 26.6.50. Familial predisposition: mother's sister died of "spinal disorder" at the age of 18 months. Only child. Pregnancy and delivery normal. Birth weight 2500-3000 g.

Symptoms: at 18 months treated for kyphosis at an orthopaedic hospital in a plaster bed. Had until then been possibly a little retarded but walked with support, said single words and was beginning to be toilet trained. Since then there had been decreasing mental and physical development. Admitted to the R.H. Paediatric Department many times, the last time at the age of 4 years *L.E.G.* at 3 years showed a ratio of 0.33 (0.31/0.34). 3rd ventricle 9 mm. Increased cortical air particularly over the Sylvian fissure. Repeat *L.E.G.*

at the age of 4 years showed a ratio of 0.32 (0.31/0.33). 3rd ventricle ? (pictures technically not very good).

Admitted to N.K. department at 4 years. Eye examination revealed atrophy of the optic nerves, possibly sequelae of chorio-retinitis. He lay with closed eyes. Musculature was poorly developed; there was pronounced spasticity of the extremities, particularly the legs, and bilateral Babinski. E.E.G. showed no definite abnormality.

V.E.G.: pressure 80, clear fluid. Ratio 0.35 (0.36/0.34). 3rd ventricle 9 mm. Pronounced cortical air. Was very ill and flaccid after the examination and there was leakage of cerebrospinal fluid for several days. Temperature 41°C . the second day and re-puncture performed. This showed no abnormality and no increase of cell contents on repeated examination. Temperature fell to normal in about 14 days.

Follow-up: admitted to a paediatric department until 4 years 2 months, then transferred to another hospital where he died a week later. He was febrile for no apparent reason. No autopsy performed.

Diagnosis: spastic paraplegia, oligophrenia (? degree), atrophy of the optic nerves, ? cerebral hyperpyrexia.

Summary: a boy whose maternal aunt died from a spinal disorder. Since the age of 18 months had increasing kyphosis and associated motor and mental retardation. L.E.G. at the age of 3 and 4 years showed a ratio of 0.33 and 0.32 respectively. V.E.G. at the age of 4 years showed a ratio of 0.35, 3rd ventricle 9 mm. After discharge he was transferred to another hospital where he died a week later in possible cerebral hyperpyrexia.

90.

N.K. no. 22448/54. Boy born 29. 11. 53. No familial predisposition. Only child. Pregnancy normal. Birth normal apart from the fact that injections were given. Birth weight 3250 g.

Symptoms: at the age of 10 days had a brief seizure during which his head fell forward and his gaze became fixed. Has since had daily series of such seizures and at the age of 3-4 months they began to be accompanied by tonic jerks in the arms. Seizures increased to 10-15 seizures in each series. Admitted to R.H. Paediatric Department almost in status epilepticus. E.E.G. showed severe abnormality with numerous diffuse spikes and waves, particularly posteriorly.

Admitted to N.K. department at the age of 10 months. Eye examination: possible blindness. Head circumference 46 cm. "Cracked pot" sound on cranial percussion. Reflex examination: no definite abnormality. Could not sit without support. X-ray of skull normal.

V.E.G.: pressure 150, clear fluid. Ratio 0.35 (0.34/0.35). 3rd ventricle 7 mm. Temperature 39.4°C . the second day, normal on the fifth. Otherwise no complaints.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department between the age of 1-2 years. Continued to have many convulsions and was severely retarded. Admitted to a State mental institution at the age of 2 years and diagnosed as a case of oligophrenia (idiocy), organic encephalopathy, hydrocephalus and epilepsy. Head circumference on admission 47 cm. Smiles when spoken to. Does not react to conversation otherwise. Has to be fed. Since said to be able to turn himself over in bed. Has many febrile colds and a poor appetite. Is miserable and apathetic. Is hypotonic and cannot sit alone. Appears completely vacant and cannot focus. No seizures. Ultimate prognosis very poor.

Diagnosis: oligophrenia (idiocy), epilepsy (? ceased), hypotonia.

Summary: a boy who started to have seizures at 10 days of age. These increased and occurred in series. V.E.G. at the age of 10 months showed a ratio of 0.35, 3rd ventricle 7 mm. Continued to have seizures and was very retarded mentally. Is in a State mental institution and making no intellectual progress.

91.

N.K. no. 23163/55. Boy born 30. 1. 49. No familial predisposition. Pregnancy and birth normal. Birth weight 3500 g.

Symptoms: at the age of 2-3 years had an episode of pallor, falling and convulsive jerks in all extremities of several minutes' duration. After two years' freedom from seizures had 3-4 similar attacks in 6 months.

Admitted to N.K. department at the age of 6 years 2 months. Eye examination normal. E.E.G: moderately severe abnormality with bi-occipital changes.

S.E.G: pressure 350, clear fluid. Ratio 0.35 (0.36/0.34). 3rd ventricle 8 mm. No increase of surface air. Temperature 38.6° C. the same day, normal on the third day.

Follow-up: has been very well since. Continues to take phenytoin but has not had any convulsions for many years. Goes to a normal school. Physical examination: healthy, normal appearance, and well-proportioned. Mental development normal. Head circumference 52.6 cm. Eyes normal. Neurological examination and motor system normal.

Diagnosis: epilepsy.

Summary: a boy who at the age of 2-3 years developed seizures which after ceasing for about two years returned at the age of 6 years. S.E.G. ratio 0.35, 3rd ventricle 8 mm. Continues to take phenytoin but has not had any seizures for a long time. Attends an ordinary school and is doing well.

92.

N.K. no. 23283/55. Boy born 7. 12. 52. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 2500 g.

Symptoms: had enteritis at the age of 20 days. At the age of 2 months had a febrile convulsion in connection with otitis. Admitted to a paediatric department on both occasions. Has had repeated convulsions since, at first febrile but since afebrile. The convulsions have been generalised and accompanied by loss of consciousness. During the months just before admission there were also petit mal attacks. Both physical and mental development were slow. Admitted to R.H. Paediatric Department at the age of 2½ years.

L.E.G: ratio 0.35 (0.35/0.35). Increased cortical air, particularly frontally. No complaints after the examination. E.E.G. showed no specific abnormality.

Admitted to N.K. department at 2 years 5 months. Eye examination: bilateral optic nerve atrophy. Shape of head rather odd with an extremely flattened forehead. Gait stumbling and legs crossed. Could not walk alone. Very restless and mentally retarded. Reflexes normal. Burr holes on both sides showed large collections of fluid beneath normal arachnoid. No sub-dural abnormality. The cortex appeared normal.

Follow-up: in reply to the questionnaire, the family indicated that visits by doctors or nurses from the hospital were not wanted, and added that information could be obtained from their own doctor in whom they had full confidence. The family doctor wrote to say that the patient was not under mental care. He had been able to walk alone since the age of 4 years and though he could not talk, his understanding was good. He could feed himself but was not toilet trained. He had no attacks of grand mal but 15-20 petit mal seizures occurred daily.

Diagnosis: epilepsy, retarded motor development, ? mental state.

Summary: a boy who since 2 months of age had repeated febrile and afebrile convulsions. Development always retarded. L.E.G. at 2 years of age showed a ratio of 0.35. Burr holes revealed sub-arachnoid fluid on both sides. Personal examination was not allowed but information was obtained from the family doctor to the effect that petit mal seizures still occurred. The child did not talk but there had been some development.

93.

N.K. no. 23330/55. Boy born 2. 2. 54. No familial predisposition. Third of three children (the first died at 9 days from intra-cranial haemorrhage). Pregnancy normal. Delivery 3 weeks premature and easy. Birth weight 3100 g.

Symptoms: when a fortnight old had projectile vomiting and was therefore admitted to hospital suspected of having pyloric stenosis but this was not proved. Weight gain was poor so he was admitted at the age of 3 months to the R.H. Paediatric Department. He was small, thin and in poor general condition. He could not focus. Subdural puncture: no abnormality. A congenital heart disorder was diagnosed. Usually lay in opisthotonus

position with the hands clenched. Re-admitted when a little more than a year old and continuous choreatic movements seen.

L.E.G.: ratio 0.35 (0.34/0.35). 3rd ventricle 6 mm. Marked increase of surface air.

Admitted to N.K. department at the age of 15 months. Burr holes just in front of the coronal suture on both sides showed no sub-dural hygroma. Cortex appeared very atrophic with large collections of fluid. Temperature was already raised before the examination, 39.3° C. the day after and normal by the 5th day. No other complaints.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. At the age of 2 years 3 months had several febrile episodes without apparent reason. Continued to vomit. Physically there appears to have been some progress. Head circumference 47 cm. Repeated *L.E.G.* ratio 0.35 (0.33/0.36). 3rd ventricle 6 mm. There is pronounced increase of surface air. *E.E.G.* shows fast activity over the vertex but no real abnormality. Application had been made for the patient to be placed under State mental care but later information was that he had died in hospital at the age of 3½ years from bronchopneumonia. No autopsy performed.

Diagnosis: spastic tetraplegia, oligophrenia.

Summary: a boy whose older sibling died at 9 days from an intra-cranial haemorrhage. When a few weeks old had projectile vomiting accompanied by poor weight gain and retarded development. *L.E.G.* at that time showed a ratio of 0.35, 3rd ventricle 6 mm. Burr holes revealed atrophic cortex with fluid collections. A later *L.E.G.* showed unchanged ratio and 3rd ventricle but a further increase in cortical air. Died in hospital at the age of 3½ years from bronchopneumonia.

94.

N.K. no. 23350/55. Boy born 17. 2. 44. No familial predisposition. First of two children. Pregnancy: no information. Child asphyxiated at birth. Birth weight normal.

Symptoms: well until a little more than 10 years old when a few days after laryngitis accompanied by high fever the patient complained of headache and sleepiness. Then became irritable, withdrawn and touchy and did not do well at school. Three weeks after laryngitis he had difficulty in understanding what was said to him but he appeared to hear well enough. Examined in the R.H. Otological Department at the age of 9½ years: either impressive aphasia or psychogenic deafness. Examined in the R.H. Child Psychiatry Department 3 months later: conversion hysteria. Admitted to the R.H. Neuromedical Department for three months at the age of 10 years. Neurological examination showed no abnormality. *L.E.G.* ratio 0.35 (0.35/0.35). 3rd ventricle 9 mm. The condition had progressed over the previous 3 months. There had been increasing behaviour difficulties and his speech had become more and more stumbling and slow and he spoke less than before. In addition he had gait difficulties. At the age of 11 years he was re-admitted to the R.H. Neuromedical Department where a clear progression of an organic brain disease was found, probably leucoencephalitis.

Admitted to N.K. department at the age of 11 years. Severe aphasia present. Hearing probably satisfactory. Legs spastic but of normal strength. Gait broad-based with a tendency to fall. Bilateral Babinski. Patellar reflexes brisk particularly on the right side. Eye examination normal. *E.E.G.* severely abnormal with right-sided predominance. X-ray of skull normal.

V.E.G.: pressure 300, clear fluid. Ratio 0.35 (0.34/0.35). 3rd ventricle 8 mm. Temperature 38° C. the same day, otherwise no complaints. Cortical biopsy did not enable a definite diagnosis to be made but raised the suspicion of encephalitis because of the finding of cell infiltration.

Follow-up: admitted to a State mental institution where he died 13 days later. On admission it was impossible to make contact with him. The right arm and leg were completely paralysed. He could not see and presumably could not hear. He had dry lips and cyanotic cheeks. Muscle tone was increased in the legs. He was no longer toilet trained. The day he died the temperature rose to 40° C. but pulmonary auscultation revealed no abnormality. The condition was thought to be a progression of the encephalitis. No autopsy performed.

Diagnosis: progressive brain disorder, possible leucoencephalopathy.

Summary: a boy who was completely well until the age of 10 years when, following laryngitis, he developed signs of a progressive brain disorder with gait and speech difficulties. L.E.G. at 11 years showed a ratio of 0.35. Repeat V.E.G. two months later showed the same findings. Cortical biopsy raised the suspicion of encephalitis. He was admitted to a State mental institution and died 13 days after admission from what was thought to be a progression of the encephalitis.

95.

N.K. no. 2868/41. Boy born 23. 12. 26. Familial predisposition: cousin is schizophrenic. Fifth of five children. Pregnancy and delivery normal. Birth weight uncertain.

Symptoms: possible skull fracture in a street accident at the age of 6 years. No loss of consciousness or other symptoms. In the four years preceding admission there were increasing generalised convulsions with accompanying loss of consciousness. At time of admission there were up to 6 such episodes during 5 days. Admitted to an epileptic hospital for a month at the age of 15 years. X-ray of skull normal. Eye examination revealed incipient papillary stasis.

Admitted to N.K. department at 14 years 10 months of age. Eye and neurological examination normal.

V.E.G.: low pressure. Ratio 0.36 (0.36/0.37), 3rd ventricle 5 mm. Normal surface air distribution. Temperature 38.8° C. after the examination and the next day, but no other complaints.

Follow-up: was admitted to an epileptic hospital on numerous occasions between the age of 15 and 29 years. Diagnosed as cryptogenic epilepsy and dementia. Four P.E.G.'s were performed at the age of 20, 23, 25 and 28 years. Ratios were 0.37 (0.37/0.38), 0.35 (0.33/0.38), 0.36 (0.35/0.38), 0.38 (0.36/0.40). Was also admitted to a neurosurgical department elsewhere at the age of 26 but no change in his condition was found. At home he had many episodes of petit mal and less frequent generalised convulsions. He was treated with anti-epileptic drugs, at times in such large doses that he became drug-intoxicated. He tried to do some kind of manual work but became rapidly exhausted. Attended school until the age of 15. Seems to be increasingly dull with loss of initiative. Has had chewing and swallowing difficulties for a while. His gait is more unsteady and he puts one foot in front of the other very slowly and almost feels his way. Occupies his time with reading, listening to the radio and smoking. Physical examination: answers slowly but fairly sensibly. Appears very confident. Head circumference 58.2 cm. Eye examination and reflexes normal.

Diagnosis: epilepsy with additional reduction of mental and motor ability; ? atrophic myotonia.

Summary: a boy who had a possible skull fracture at the age of 6 years. From the age of 11 had increasing generalised convulsions. V.E.G. at 14 years showed a ratio of 0.36, 3rd ventricle 5 mm. Admitted on several occasions to an epileptic hospital and repeated P.E.G.'s showed a ratio around 0.37. He is at home, cannot work and appears to be losing all initiative. Has chewing and swallowing difficulties and his gait is unsteady.

96.

N.K. no. 00104/48. Boy born 28. 1. 45. Familial predisposition: father's sister feeble-minded. Second of two children. First child died of whooping-cough at the age of 7 months. Pregnancy complicated by hypertension. Birth normal. Birth weight 3100 g.

Symptoms: at the age of 2 years it was noticed that he was dragging one leg. His gait became worse and by the time he was 3 years old he could hardly walk at all. This was followed by further motor deterioration and his speech decreased. Admitted to hospital.

Transferred to N.K. department at the age of 3 years. Eye examination normal. "Cracked pot" sound on cranial percussion. Head circumference 52 cm. Stood and walked very unsteadily. X-ray of skull showed slight gaping of the sutures with increased digital markings. Neurological examination revealed a right spastic hemiparesis.

V.E.G.: pressure 150, clear fluid. Ratio 0.36 (0.36/0.35). 3rd ventricle 3 mm. Temperature 38.3° C. the following day, normal the next day.

Follow-up: the condition progressed with regard to motor difficulties and speech disturbance. Mentally the patient was difficult to assess but he was presumably normal. There were no typical convulsions. L.E.G. was performed twice, ratio 0.37 (0.36/0.38). He died suddenly during admission to a treatment home. Autopsy: no abnormal findings except in the brain. There were symmetrical changes in the basal ganglia, medulla oblongata and spinal cord at different stages of development.

Diagnosis: progressive brain disorder, rigidity and dysarthria.

Summary: boy with mental retardation in his father's family. Pregnancy was accompanied by hypertension. From the age of 2 years he had progressive motor and speech disturbance. V.E.G. at 3 years showed a ratio of 0.36, 3rd ventricle 3 mm. The condition steadily progressed, and he died suddenly without obvious explanation for the cause of death.

97.

N.K. no. 04227/49. Boy born 17.1.48. No information available on familial predisposition. Third of three children. Pregnancy: toxæmia during the first few months. Birth precipitate. Birth weight 3750 g.

Symptoms: when about 18 months old he became very restless and irritable. Shortly after this he had 3-4 days of severe vomiting without diarrhoea. Admitted to infectious diseases hospital where he was crying, irritable, sucking his lips and grating his teeth. Vomiting continued. Eye examination showed blurring of the discs and a small haemorrhage temporally on the right side. Two lumbar punctures showed no abnormality.

Admitted to N.K. department at the age of 19 months. Eye examination: bilateral papilloedema. Head circumference 50 cm. "Cracked pot" sound on percussion. Doubtful bilateral Babinski. X-ray of skull: suture springing, otherwise no abnormality. E.E.G. not done.

V.E.G.: pressure 100, clear fluid. Ratio 0.33 (0.32/0.35). 3rd ventricle ? Left side - 5 mm. No complaints after the examination.

S.E.G.: pressure 400. Ratio 0.36 (0.35/0.36). 3rd ventricle 12 mm. Temperature 37.8° C. otherwise no complaints.

Follow-up: attends a normal school and is doing very well indeed. Has had no further trouble since admission. Physical examination: completely healthy. Head circumference 54 cm. Sight and hearing normal. Reflexes normal. Power good.

Diagnosis: healthy.

Summary: boy who had a precipitate delivery. At 18 months of age he became restless and irritable and later had severe vomiting. V.E.G. at 18 months showed a ratio of 0.33, and repeat S.E.G. showed a ratio of 0.36, 3rd ventricle 12 mm. At follow-up he was attending a normal school and was completely healthy.

98.

N.K. no. 04925/50. Boy born 20.5.49. Familial predisposition: mother feeble-minded, father a criminal. Third of three children. No information on pregnancy. Birth said to be premature. Birth weight 2650 g.

Symptoms: lived in a nursery home. At 6 months of age he was noticed to have a large head. Shortly afterwards he was febrile and had a cold and indigestion. Admitted to hospital at 6 months with otitis media. Skull X-ray and eye examination showed no abnormality. There was gain in weight and he could grasp. Could not sit without support.

Admitted to N.K. department at the age of 8 months. Eye examination normal. Head circumference 45 cm. Motor co-ordination good. Reflexes normal. Sub-dural puncture: clear fluid. V.E.G. unsuccessful.

S.E.G.: pressure 700. Ratio 0.36 (0.38/0.34). 3rd ventricle 6 mm. Ventricles separated from each other so that accurate measurement could not be made but there was definite cortical atrophy, particularly frontally and corresponding to the Sylvian fissure. Temperature 38.5° C. the same day, normal on the third day. Otherwise no complications.

Follow-up: developmental quotient at the age of 10 months was 94, at 3 years 82, 5 years 70, 6 years 52 and 7 years 70. Stayed in various nursery homes and is now in a

special municipal nursery home. Began to talk at the age of 3 years. Somewhat unresponsive but apparently sensible enough. Had made great progress but was still stereotyped in his behaviour. Had been having speech therapy without any real success. Physical examination: appeared rather slow and reserved but otherwise not mentally abnormal. Head circumference 54.4 cm. Hearing normal. Eye examination normal. Speech hesitant. Reflexes normal. He would not jump without support.

Diagnosis: intellectual inferiority (? pseudo), ? "non-talker-non-jumper" syndrome.

Summary: boy with a familial predisposition for mental retardation. At the age of 6 months he was noticed to have a large head. S.E.G. ratio 0.36, 3rd ventricle 6 mm. Increased cortical air present. Over the following years he spent his time in various nursery homes. Psychological development was at first retarded but is now improving. He has speech difficulties and cannot jump without support.

99.

N.K. no. 05178/50. Girl born 25. 5. 43. Familial predisposition: nervousness in family. Fourth of four children and is twin B, a heterozygotic twin. Pregnancy normal. Asphyxia at birth. Birth weight 2000 g.

Symptoms: decreasing bronchitis since infancy. Many attacks of otitis media. 10 months before admission to N.K. department sustained a fractured skull when she fell downstairs. No symptoms except for a squint the day after. Admitted to hospital where the diagnosis was verified by skull X-ray. 8 months before admission to N.K. department admitted elsewhere because of right-sided otitis media and temperature above 40° C. After discharge there were character changes. She cried more easily, trembled all over, was nervous and could not get on with her brothers and sisters. Had 3-4 temper tantrums and complained of headache localised to the forehead.

Admitted to N.K. department at the age of 6 years 9 months. Eye examination showed possible convergent squint and slight hypermetropia. Reflexes normal. Mental state normal. X-ray of skull showed it to be thin-walled with increased digital markings and increased frontal venous grooves. E.E.G. normal.

S.E.G.: pressure 180. Ratio 0.36 (0.34/0.38). 3rd ventricle 5 mm. There was an ill-defined sub-dural air collection over the right occipital pole. Temperature 38.4° C. the same day, otherwise no complaints.

Follow-up: was admitted to the R.H. Paediatric Department at the age of 9 years for investigation of possible precocious puberty. She had grown a great deal and was miserable and depressed. E.E.G. and neurological examination normal. L.E.G. did not give good pictures but on one of them the ratio on the left side could be measured to 0.39. The patient is now much better and is more sociable. She has only occasional slight headache localised to the left side of the forehead. The other twin is word blind and attends the Speech Institute. The patient has always had difficult feet and wears stiff shoes. Is in the appropriate class at school for her age. Physical examination: head circumference 57.2 cm. Finger-finger and finger-nose tests normal. Eye examination and reflexes normal. Motor system, balance and co-ordination normal. Is in full puberty.

Diagnosis: temper tantrums (decreasing), puberty.

Summary: girl who is twin B and who was asphyxiated at birth. At the age of 6 years sustained a fractured skull after which character changes occurred. S.E.G. when nearly 7 years old showed a ratio of 0.36, 3rd ventricle 5 mm. At the age of 9 years admitted for investigation of possible precocious puberty but no abnormality was found. At present the headaches and temper tantrums are decreasing and she is physically healthy.

100.

N.K. no. 05539/50. Boy born 15. 6. 46. No familial predisposition. Second of three children. Pregnancy and delivery normal. Birth weight 2700 g.

Symptoms: when 3½ years old had 3-4 generalised convulsions of unknown origin during 2 weeks followed by numerous attacks of petit mal. Was irritable and unmanageable at the same time. Admitted to epileptic hospital at the age of 4 years. E.E.G. difficult to assess but showed epileptiform changes. Gait characterised by left-sided hemiplegia.

Admitted to N.K. department at the age of 4 years. Eye examination normal. Left-sided hemiplegic movements on walking but no reflex changes. X-ray of skull: deep posterior fossa. E.E.G.: severe dysrhythmia with diffuse spike-wave formations.

S.E.G.: pressure 330, clear fluid. Ratio 0.36 (0.35/0.37). 3rd ventricle not measurable. Normal surface air. No complications after the examination.

Follow-up: admitted to epileptic hospital many times, for six months when aged 4 and another six months two years later. Diagnosed as a case of epilepsy and sequelae of encephalitis. Admitted at the age of 6 years because of continuing convulsions twice a day. On physical examination the patient was found to be flaccid but otherwise normal. Co-operation during the examination was poor. L.E.G. showed a ratio of 0.42 (0.40/0.44). Right side - 5 mm. 3rd ventricle 5 mm. E.E.G. showed very severe dysrhythmia with many spike-waves. Was very much better after the insufflation. No attacks since that time. Still takes ephedrine and phenobarbitone in small doses. Has been in an exam-free school for 3 years. It is the general opinion that he may show some "gaps" but is otherwise completely fit. Has made up a great deal of what he lost between 3-6 years. Physically entirely normal. Physical examination: head circumference 56 cm. Eye examination normal. Reflexes: ankle clonus on the right side. No Babinski. Patellar reflexes normal. Arms entirely normal. Fast movements performed without difficulty. Psychologically appears to be normal for his age.

Diagnosis: healthy, previous epilepsy.

Summary: a boy who at the age of 3½ years had generalised convulsions and petit mal. Walked with left-sided hemiplegic movements. S.E.G. at the age of almost 4 years showed a ratio of 0.36. Continued to have periodic convulsions until the age of 6 years when L.E.G. was performed and showed a ratio of 0.42, 3rd ventricle 5 mm. No seizures since this time. He has continued to improve and is now perfectly normal apart from a few gaps corresponding to the period of illness between 3-6 years.

101.

N.K. no. 06238/50. Boy born 30.7.50. Familial predisposition: mother's brother had cerebral haemorrhage at the age of 3 months and is in a State mental institution. Only child. Pregnancy normal. Delivery difficult, caudate position with manual extraction. Asphyxia lasted 20 minutes. Birth weight 3650 g.

Symptoms: was very sick for the first few days with crying, vomiting and cyanosis. Fontanelles bulged. Pronounced rigidity of both legs. At the age of 23 days he was improving and the rigidity decreasing. A fracture of the right clavicle had healed in a good position. Admitted to the R.H. Paediatric Department where alternating rigidity and flaccidity was found. Daily sub-dural punctures with withdrawal of 10-20 ml. usually bloodstained fluid, especially from the left side. X-ray of the skull and eye examination normal.

Admitted to N.K. department at the age of two months. Babinski present and patellar reflexes elicited over an extended area. E.E.G. not done. Sub-dural puncture: clear fluid.

V.E.G.: pressure 0. Large, multilocular porencephaly in the right frontal region, communicating with the lateral ventricle. Ratio not measurable on the right side, 0.36 on the left. 3rd ventricle? Only a small ridge of surface air. No temperature rise or other complaints after examination.

Follow up: Admitted to a State mental institution from the age of 3½-4 years and then to family care until the age of 5½. Since in State institution again. Diagnosed as an idiot (I.Q. about 20), porencephaly of right frontal lobe. Physical examination: head circumference 46.8 cm. He grates his teeth and chews his fingers. No real contact made with the patient who does not say anything. He is very rigid but not really spastic. No ankle clonus. Becomes very stiff on being touched. Cannot walk or stand without support. Hearing appears normal. Sight difficult to assess.

Diagnosis: oligophrenia (idiocy), rigidity.

Summary: a boy whose maternal uncle is in a State mental institution. Birth difficult, of long duration and accompanied by asphyxia. Rigid since birth. V.E.G. at the age of two months showed a ratio measurable only on the left side, 0.36, and a large multilocular

porocephaly in the right frontal region, communicating with the lateral ventricle. Is in a State mental institution. Has a very low I.Q. and is still rigid.

102.

N.K. no. 07856/51. Girl born 13. 3. 51. No familial predisposition. Second of two children (twin B). Pregnancy normal. Birth 6 weeks premature. No asphyxia. Twin A was macerated. Birth weight 1500 g.

Symptoms: admitted to hospital immediately after birth. Did well. Developed bronchopneumonia at the age of 6-7 weeks and was transferred to a medical department where she was found to have too large a head and widened sutures. X-ray of skull showed no abnormality.

Admitted to N.K. department at the age of 5 months. Head circumference 41.5 cm. Reflexes normal. E.E.G. not done.

V.E.G.: pressure 140, clear fluid. Ratio 0.36 (0.35/0.37). 3rd ventricle 6 mm. No complications after the examination.

Follow-up: had a convulsion in connection with tonsillitis and high fever at the age of a year. This was repeated the next year. Stood with support at the age of 7½ months and alone at 16 months. Walked alone at 18 months and said single words at 17 months. Development normal and memory good. Physical examination: head circumference 53.5 cm. Slight convergent squint present. Face and head shape that of a premature child. Reflexes brisk but probably not pathological.

Diagnosis: previous febrile convulsions, healthy.

Summary: girl, second twin. The other twin was macerated. Birth weight 1500 g. Increasing head circumference led to V.E.G. being performed. Ratio 0.36, 3rd ventricle 6 mm. Somewhat slow motor development and two episodes of febrile convulsions. Perfectly well at follow-up.

103.

N.K. no. 08350/51. Boy born 28. 3. 51. No known familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3100 g.

Symptoms: severe jaundice from the first 24 hours until one month of age. Haemoglobin fell to 62% and repeated transfusions had to be given. On admission to the R.H. Paediatric Department it was noticed that he was alternately rigid and flaccid and often cried. X-ray of skull normal.

Admitted to N.K. department at the age of 8 months. Eye examination showed a divergent squint. Head circumference 42 cm. Lay with head to the right side. Could not focus or sit up. Intermittent rigidity present in arms and legs. Bilateral Babinski. Brisk tendon reflexes.

S.E.G.: pressure 320, clear fluid. Ratio 0.36 (0.36/0.36). 3rd ventricle 15 mm. Increased cortical air on the right side.

Follow-up: admitted several times to a paediatric department, at the age of 9 months and 10 months because of fever in connection with pneumonia. Admitted last at the age of 19 months and was dead on admission. Had again had high fever to 42°C. for two days. Autopsy: ? suffocation, pulmonary atelectasis (almost one-third of the lung), hyperaemia of the meninges.

Diagnosis: sequelae of foetal erythroblastosis, cerebral palsy (rigidity), fever of presumed cerebral origin.

Summary: boy who was severely jaundiced for a month after birth and had intermittent rigidity. S.E.G. at 8 months showed a ratio of 0.36, 3rd ventricle 15 mm. Increased cortical air. Died after high fever at the age of 19 months.

104.

N.K. no. 08786/52. Boy born 19. 7. 49. No familial predisposition. Only child. Pregnancy normal. Birth two months premature. No asphyxia. Birth weight 1850 g.

Symptoms: severe jaundice at birth. Admitted to a paediatric department. Large head circumference noticed at the age of a year. Investigated in the R.H. Paediatric Department

at the age of 16 months. Developmental quotient 48. X-ray of skull: large but otherwise normal. Eyes: hypermetropia. L.E.G: considerable dilatation of the ventricular system.

Admitted to N.K. department at the age of 2 years 9 months. Eye examination showed convergent squint. Head circumference 53 cm., flattened posteriorly. Stood with support with adducted legs and slight equinus deformity. Legs appeared somewhat rigid. Bilateral Babinski. Brisk tendon reflexes in the legs. E.E.G. not done. Burr holes showed no fluid.

S.E.G: pressure 300, clear fluid. Right-sided ratio not measureable because of missing internal cranial diameter. Ratio on the left 0.36. Further pictures showed that the skull was not asymmetrical. By calculation it was found that the ratio was 0.36 (0.37/0.36). 3rd ventricle 15 mm. Increased cortical air. Temperature 38.8° C. the same day, normal on the third day. Otherwise no complaints.

Follow-up: attends the R.H. Paediatric Department as an out-patient. Still retarded from the point of view of motor ability. Was thus at the age of 7 years only able to walk in a walking-chair and take a few steps holding on to parallel bars. Behaviour is very childish and he makes many funny little remarks. Physical examination: head circumference 54 cm. Only slight reflex changes in the arms but increased muscle tone and pronounced reflex changes in the legs. Places his feet in equinus position. Speech is quite good.

Diagnosis: oligophrenia (debilitas mentis or imbecility?), sequelae of jaundice and prematurity, tetraplegia (? spastic paraplegia).

Summary: a boy who was born two months prematurely and was jaundiced. Because of retarded development and an increased head circumference S.E.G. was performed at the age of 2³/₄. Ratio 0.36, 3rd ventricle 15 mm. Is still mentally and physically retarded and has a possible spastic tetraplegia.

105.

N.K. no. 20211/53. Girl born 15.8.49. No definite familial predisposition. Only child. Pregnancy and birth normal. Birth weight 4000 g.

Symptoms: after laryngitis at about 18 months of age with high fever but without cerebral symptoms there was gradual mental and physical deterioration. Could not definitely recognise her parents. In the months before admission had daily screaming attacks. Had ceased to be toilet trained and could not chew. Admitted to the R.H. Paediatric Department at the age of 2 and 3 years. E.E.G. normal. L.E.G. ratio 0.36 (0.34/0.38). 3rd ventricle 6 mm. No increase of surface air. Developmental quotient 37.

Admitted to N.K. department at the age of 3 years 5 months. Severely oligophrenic. Eye examination normal. Head circumference 47.4 cm. All extremities flaccid and hypotonic. Periodically increased tone in the extensors. No ankle clonus or Babinski. She performed ataxic almost athetoid movements with the arms. Biopsy: the dura was opened and there appeared to be increased fluid beneath it. There also appeared to be cortical atrophy. Microscopy: cortex with a variably severe degree of ganglion cell loss. No complaints after the examination.

Follow-up: had been in a State mental institution since the age of 4 years 3 months, diagnosed as a case of oligophrenia (idiocy). Had been an easy and manageable child. Often had febrile episodes and had had one attack of acute exudative left-sided pleurisy. There had been one episode of spasmodic jerks in the face and both arms. No intellectual progress had been made. Physical examination: extremely rigid. It was not possible to make any contact with the child and the rigidity increased when she was touched. She made constant "pill-rolling" movements with her fingers. Head circumference 47.6 cm. Eye examination normal. Could make sounds but said no distinguishable words. Reflexes somewhat brisk with an occasional jerk on testing for ankle clonus but this was probably not pathological.

Diagnosis: oligophrenia (idiocy), possible epilepsy, rigidity, (? basal ganglia lesion).

Summary: a girl who deteriorated mentally and physically after laryngitis at the age of 18 months. L.E.G. when 3 years old showed a ratio of 0.36, 3rd ventricle 6 mm. Biopsy showed possible cortical atrophy. Is now in a State mental institution. Is severely oligophrenic and rigid and makes constant "pill-rolling" movements with the hands.

106.

N.K. no. 20597/53. Girl born 13. 6. 52. No familial predisposition. Second of two children (first was still-born). Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: at the age of 5 months stiffened at though in a seizure and this lasted a few minutes and was followed by 5-7 such attacks daily. During the month before admission, however, there had been no seizures. There appeared to be no after-effects and she was as bright and lively as other children. Admitted to the R.H. Paediatric Department at the age of 9 months. Petit mal seizures noticed. X-ray of skull and eye examination normal. Sub-dural puncture also normal. E.E.G. abnormal with a focus over the right temporal region.

Admitted to N.K. department at the age of 9 months. Eye examination normal. Very restless. Developmental quotient 63. E.E.G. showed bilateral spikes, mostly temporally and on the right side.

S.E.G: pressure 210, clear fluid. Ratio 0.36 (0.33/0.38). 3rd ventricle 7 mm. Surface air in the form of large and small air collections, particularly frontally. No fever or other complications following the examination.

Follow-up: followed up in the R.H. Paediatric Department. No seizures recently. At the age of almost 3 years could not say any distinguishable words but chattered a great deal. Walked a lot and was constantly on the move. Physical examination: head circumference 47.9 cm. Convergent squint present. Variable bilateral Babinski. Would appear to be a child with late motor and mental development.

Diagnosis: retarded development, motor and mental; oligophrenia (intellectual inferiority or debilitas mentis); epilepsy.

Summary: a girl who between 5 and 8 months had 5-7 daily seizures during which she stiffened. S.E.G. at 9 months showed a ratio of 0.36, 3rd ventricle 7 mm. At follow-up her speech development had been slow but she was making continued progress and was considered to be a late developer.

107.

N.K. no. 1660/39. Boy born 17. 8. 25. No familial predisposition. Third of three children. Pregnancy: nothing abnormal except for a descended uterus. Birth normal. Birth weight 4000 g.

Symptoms: sustained a head injury when about 8 years old when he fell from a car on to the pavement. There was no loss of consciousness. Some two months later became bad-tempered and irritable but continued to attend school. Two weeks later developed aphasia and right-sided hemiplegia. The hemiplegia never entirely disappeared. During the two years preceding admission he had right-sided epileptic convulsions with variable loss of consciousness. The convulsions lasted about 2-3 minutes. Increased in frequency and at the time of admission were occurring as many as nine times daily and the hemiplegia had become more pronounced. Admitted to hospital and transferred.

Admitted to N.K. department at the age of 14 years. Small and thin child. Eye examination normal. Doubtful paresis of the right facial nerve. Slight spastic paresis of the right arm but no definite paresis of the legs. Right-sided dysidiadokokinesis and Babinski. X-ray of skull showed brachycephaly and a fracture. Left-sided arteriography: a large number of vessels and the whole media group appeared lifted forward.

V.E.G: the pictures were not definitely measureable but the dilatation appeared equal on both sides. Ratio on the left side 0.37. Temperature the same day was 38.2° C. Otherwise there were no complications.

Follow-up: admitted to a neurological department at the age of 27 years because of Jacksonian seizures which had occurred at about yearly intervals. Findings were as before with a right-sided hemiplegia. E.E.G. showed slight dysrhythmia without focal changes. L.E.G: incomplete filling of the ventricular system. Lateral ventricles slightly dilated but in normal position. No seizures since his last admission except for two minor episodes in connection with a change of medicine. Has trained as a bookbinder and works full-time in a special factory where he is doing very well. Is married. Right-sided spastic hemiplegia continues but the patient can use his right hand without difficulty. Physical examination: head circumference 58 cm. Motor system completely normal. Reflex

changes corresponding to the right spastic hemiplegia and more pronounced in the arm than the leg.

Diagnosis: Jacksonian epilepsy; right-sided spastic hemiplegia.

Summary: boy who sustained a head injury at the age of 8 years. This was followed by hemiplegia and an increasing number of right-sided Jacksonian seizures. V.E.G. at 14 years showed a ratio of 0.37. At follow-up he still had slight hemiplegia but only very rare seizures. He was married and working full-time.

108.

N.K. no. 8688/46. Boy born 3.2.42. No familial predisposition. First of two children. No information available on pregnancy. Delivery normal. Birth weight 3200 g.

Symptoms: had always been rather retarded but this was not definitely confirmed until about the age of 3 years. During the year before admission he became difficult, could not understand and was bad-tempered and unreasonable. Four months before admission had episodes of petit mal and one month before lost consciousness twice for 6-7 minutes with incontinence of urine. Admitted to a paediatric department where no seizures were seen but he appeared to have behaviour difficulties. X-ray of skull normal.

Admitted to N.K. department at the age of 4 years 7 months. Head circumference 53 cm. Eye examination showed no definite abnormality. Speech indistinct. He was very unmanageable. Neurological examination normal. E.E.G. not done.

S.E.G: pressure 120, clear fluid. Ratio 0.37 (0.37/0.38). 3rd ventricle 4 mm. No increase of cortical air. Temperature 38.5° C. No other complications.

Follow-up: was admitted to a paediatric department on two occasions. No seizures were seen but his psychological difficulties had increased. He was referred to the R.H. Child Psychiatry Department and from there to State mental care. He disappeared from home when 5 years old and was seen walking alone near the harbour. Footprints were seen leading out to a hole in the ice and his body was found six weeks later. Verdict at inquest was accidental drowning. No autopsy performed.

Diagnosis: psychological difficulties, ? oligophrenia, ? epilepsy.

Summary: a boy who was always said to be retarded. At the age of 3 years developed behaviour difficulties and later had epileptic seizures. S.E.G. ratio 0.37, 3rd ventricle 4 mm. Was later transferred to State mental care. Drowned when he fell through a hole in the ice.

109.

N.K. no. 06449/50. Boy born 29.1.50. Familial predisposition: sister said to have a large head. Second of two children. Pregnancy and delivery normal. Birth weight 3600 g.

Symptoms: was placed in a nursery home shortly after birth where he was thought to have a large head. Admitted to a paediatric department at the age of 7 months. No basis for hydrocephalus. Was very flaccid the whole time and could not sit alone. Psychological development normal.

Admitted to N.K. department at the age of 9 months. Eye examination normal. Head circumference 47.5 cm. Was noticeably flaccid and could not sit alone and his head was unsteady. Reflexes normal. X-ray of skull showed the cranial bones to be very thin. E.E.G. normal. Anterior fontanelle puncture showed no haematoma.

V.E.G: pressure 110, clear fluid. Ratio 0.37 (0.37/0.37). 3rd ventricle 3 mm. Temperature 38° C. the same day, otherwise no complications.

Follow-up: returned to family care when two years old. Had developed entirely normally. Was a little slow in learning to talk however. Treated for 3 years because of flat feet. Had had no seizures. Physical examination: completely normal appearance. Mental development corresponded to age. Head circumference 55.2 cm. Eye examination normal. Neurological examination normal. Pronounced pes planus deformity present.

Diagnosis: healthy, large head circumference.

Summary: a boy who was thought to have an increased head circumference (familial) and to be physically retarded. V.E.G. at 9 months showed a ratio of 0.37, 3rd ventricle 3 mm. Head still large but otherwise no abnormality present.

110.

N.K. no. 07550/51. Boy born 21. 6. 37. Familial predisposition: father's sister had epilepsy. Pregnancy and delivery normal. Birth weight 3375 g.

Symptoms: admitted when nearly 13 years old to hospital because of meningo-encephalitis. Was unconscious and had convulsions. After this was well for a year and then had increasing petit mal seizures giving place to tonic convulsions several times a week. Sustained a head injury when he fell off his bicycle during such an attack. Admitted to hospital and later to epileptic hospital. E.E.G. findings were doubtful. L.E.G: septum pellucidum cyst measuring 8 mm. Ratio 0.38 (0.39/0.37, uncorrected).

Admitted to N.K. department at 14 years of age. Eye examination revealed unequal pupils. Reflexes normal. Appeared slow and heavy. X-ray of skull: fairly well-defined venous grooves. Anterior clinoid process appeared atrophic. E.E.G: severe bilateral dys-rhythmia with doubtful right-sided preponderance.

V.E.G: pressure 80, clear fluid. Septum pellucidum cyst as found previously at the epileptic hospital, size about 12 mm. Ratio 0.37 (0.38/0.36). If corrected for the cyst the ratio became 0.30/0.30. Felt ill after the examination, had nausea and vomiting. Given saccharose without much effect. Temperature 38.6° C. the following day, normal by the 4th day.

Follow-up: had been in an epileptic hospital with occasional short periods at home. Continued to be slow and heavy and had febrile episodes. When at home could not occupy himself. I.Q. at the age of 14 years was 81. During admission at the age of 16 a new L.E.G. was performed. Ratio 0.38 (0.40/0.37), cyst 14 mm. Last admitted at the age of 18 years after having a febrile episode at home. On admission had pneumonia and went steadily downhill. The condition was thought to be primarily cerebral in origin. Just before death there was a sharp rise of temperature and Cheyne-Stokes' breathing. He died at the age of 18 years 4 months. Autopsy was not permitted.

Diagnosis: epilepsy, psychological difficulties, repeated fever.

Summary: a boy with epilepsy in his father's family. When nearly 13 years old he had meningo-encephalitis with convulsions. V.E.G. ratio 0.37, septum pellucidum cyst 12 mm. Was repeatedly admitted to epileptic hospital and had many febrile episodes and convulsions. L.E.G. at 16 showed a ratio of 0.38. Died in hyperpyrexia at the age of 18 years.

111.

N.K. no. 09229/52. Boy born 5. 7. 51. Familial predisposition: mother treated for Graves' disease since 1946. Fourth of four children. During pregnancy the mother was tired and unwell and there was weight loss. Birth normal. Birth weight 3100 g.

Symptoms: had difficulties with breast feeding but otherwise had no illness until the age of 6 months when he had a cough, pneumonia and fever for about a month. Admitted to hospital and transferred to the R.H. Paediatric Department where he was found to be flaccid and to have a large head. Right-sided sub-dural puncture showed clear fluid with some erythrocytes. Left-sided fluid was clear with fewer erythrocytes. X-ray of skull showed it to be somewhat large but otherwise normal. E.E.G. normal.

Admitted to N.K. department at the age of 11 months. Head circumference 48 cm. Eye examination normal. "Cracked pot" sound on cranial percussion. Generalised flaccidity with the legs flexed maximally at the hips and knees. Reflexes normal. Appeared alert, smiled and grasped objects. X-ray of skull: the floor of the anterior cranial fossa sloped backwards and the sutures were slightly widened.

V.E.G: pressure 100, clear fluid. Ratio 0.37 (0.36/0.38), 3rd ventricle 4 mm. Temperature 38.6° C. the same day, normal the following day.

Follow-up: discharged to a hospital for infectious diseases because of exposure to measles. Was very miserable but improved. Walked at 26 months and talked about 2 years. Contracted poliomyelitis and was admitted to hospital. Was very ill and had to learn to walk again. Perspired very easily and ran a temperature for no apparent reason. Never had convulsions. Physically normal, could walk and jump without difficulty. Speech and sensory system normal. Physical examination: head circumference 56 cm. Neurological

and eye examination normal. Had slight difficulty in balancing on one leg. Mentally appeared completely normal.

Diagnosis: unstable temperature regulation, otherwise healthy.

Summary: a boy whose mother was under treatment for Graves' disease. At the age of 6 months he had a cough and fever and when admitted to hospital was found to have an increased head circumference and flaccidity. V.E.G. at 11 months showed a ratio of 0.37, 3rd ventricle 4 mm. After poliomyelitis he was again in very poor general condition but recovered. At follow-up no abnormality was found except for unstable temperature regulation.

112.

N.K. no. 23156/55. Girl born 9. 8. 53. No familial predisposition. Third of three children. Pregnancy normal. Delivery difficult because of narrow pelvis. Birth weight 3000 g.

Symptoms: at the age of 7 months had a cold and otitis media. Some days later had convulsions in the arms and legs. Admitted to hospital where acute encephalitis was diagnosed. Lumbar puncture normal. E.E.G. abnormal in that there was no activity. Had a high temperature for 11 days and was unconscious for the same length of time. Had begun to sit up and reach for toys before she was ill. Examined in the R.H. Paediatric Department at the age of 15 months when she could sit only with considerable support. Head circumference 44 cm. Spastic tetraplegia mainly affecting the arms present. L.E.G. ratio 0.37 (0.39/0.34). 3rd ventricle 12 mm. Frontally there was increased air as seen in porencephaly.

Admitted to N.K. department at the age of 19 months. Burr hole over the right frontal region showed the arachnoid to be thickened and adherent to the dura. Entry was made into a small non-communicating cyst which contained a few drops of yellow fluid. Operation on the right side frontally: dura opened and beneath this was found a thick membrane. Beneath this again was fluid. An inner membrane was about 1 mm. thick. As much as possible of the membrane was removed so that at least the motor region was freed. At later operation on the left side a 3 mm. thick layer of membrane was removed but no hygroma was present. There was a large fluid collection under the arachnoid. Microscopy showed outer and inner membrane from sub-dural haematoma without sign of infection. After the examination temperature was 38.2° C., and after the first operation 39.1° C., and 38.8° C. on the day of the second operation.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Head circumference at the age of 2 years 9 months was 43.8 cm. Pronounced rigidity. Could not hold up her head and was severely spastic. E.E.G. severely abnormal with spike formation. Patient died at the age of 5 years 10 months. Autopsy: sub-dural membranes. No signs of infection on microscopy. *Diagnosis:* microcephaly and microgyri, bilateral sub-dural haematoma.

Diagnosis: spastic tetraplegia, oligophrenia (idiotcy).

Summary: a girl whose delivery was difficult because of the mother's narrow pelvis. At the age of 7 months she had a febrile episode with convulsions which was said to be encephalitis. Development was retarded subsequent to this and she developed a spastic tetraplegia. L.E.G. at 15 months showed a ratio of 0.37, 3rd ventricle 12 mm. Operation on both sides revealed sub-dural haematomas. No improvement following operation. Died at the age of 5 years 10 months.

113.

N.K. no. 23306/55. Girl born 14. 5. 54. Familial predisposition: mother's brother died in a State mental institution 14 years before patient's birth. Second of two children. Pregnancy normal. Delivery 4 weeks premature. Difficult but no asphyxia. Birth weight 2500 g.

Symptoms: After a stay in hospital at the age of 6-7 months the mother thought that the child was more sick and was not developing. She would not use her hands and could hardly lift her head. On admission to the R.H. Paediatric Department at the age of about 11 months she could only sit alone for a minute and had a spastic tetraplegia.

Head circumference 42 cm. She lay in opisthotonus position but had no convulsions. E.E.G. severely abnormal. L.E.G. ratio 0.39 (0.41/0.36). 3rd ventricle 8 mm. Greatly increased surface air, more pronounced on the right side.

Admitted to N.K. department at the age of one year.

V.E.G.: pressure 20, clear fluid. Ratio 0.37 (0.40/0.35). 3rd ventricle 7 mm. Increased surface air, on that occasion more pronounced on the left side. Temperature 38.6° C. the day after the examination, normal on the third day. Otherwise no complications. Cortical biopsy from the right occipital region revealed slight chronic ganglion cell changes.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Is in a nursery home under State mental care. Has no convulsions but continues to lie in opisthotonus position though this tendency is decreasing. Can follow things with her eyes and is said to recognise the nurses. Seldom smiles or reaches after things. Likes to be handled but does not co-operate in exercises. At the age of a little more than 2 years has a head circumference of 42.5 cm.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, microcephaly.

Summary: a girl whose uncle was mentally retarded and whose birth was difficult. At the age of 6-7 months development was thought to have ceased and she started to assume opisthotonus position. *V.E.G.* at the age of about a year showed ratio of 0.37, 3rd ventricle 7 mm. Biopsy showed slight ganglion cell changes. Was placed under State mental care. Appears to be severely retarded and microcephalic.

114.

N.K. no. 23452/55. Girl born 17.3.55. Familial predisposition: an older brother is in a State mental institution. Seventh of seven children. Pregnancy normal. Birth very fast but otherwise normal. Birth weight 3200 g.

Symptoms: at the age of 3 days had 4 convulsions with jerks in the arms. Eyes turned to the side. Admitted to hospital for a week and shortly after admission had another similar attack. Treated with phenobarbitone without effect. The convulsions increased in frequency and she was therefore admitted to the R.H. Paediatric Department at about 3 months of age. Examination of the heart revealed a systolic murmur. Neurological examination: Babinski and pathological patellar reflexes. There were numerous seizures with shaking and spasm. Sub-dural puncture, X-ray of skull and eye examination normal. E.E.G. possible changes.

Admitted to N.K. department at the age of 3 months. E.E.G. normal.

V.E.G.: clear fluid, pressure 25. Ratio 0.37 (0.37/0.37). 3rd ventricle 4 mm. Temperature 37.9° C. the same day. Burr holes shortly after revealed no sign of hygroma. Arachnoid was normal. Attempts were made to remove the rather large sub-arachnoid fluid collections. Temperature 39.4° C. the day after examination, normal on the third day.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. No seizures and the family thought there had been progress. Head circumference at the age of 18 months was 43 cm. Had difficulty in holding head up. Convergent squint and nystagmus present. Muscle tone not definitely altered. Tendon reflexes brisk in the arms. Plantar reflexes atypical. The family did not wish application for the child to be placed under State mental care to be made at that time but they were fully conversant with the situation.

Diagnosis: epilepsy, oligophrenia (imbecility), microcephaly.

Summary: girl whose brother is in a State mental institution, and whose birth was precipitate. From the age of 3 days she had convulsions during which her arms jerked and her eyes turned to the side. *V.E.G.* ratio 0.37, 3rd ventricle 4 mm. Burr holes showed increased sub-arachnoid fluid collections. She has since made some progress and is seizure-free. She is microcephalic and severely retarded.

115.

N.K. no. 5035 a/44. Girl born 9.8.32. No known familial predisposition. Second of three children. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: tubercle bacilli cultured from gastric washings at the age of 18 months. There had also been a chronic otitis and at the age of 2½ an operation was performed on the right ear. Since the age of 2 years 4 months there had been a total of 5 convulsions and she was admitted to hospital for this reason. The seizures were prolonged, the first being left-sided and the later ones generalised.

Admitted to N.K. department at the age of 5 years. Eye examination normal. Otological examination: apparently no hearing on the right side where foul-smelling pus was present. Mentally the patient appeared slow but answered adequately enough. Reflexes normal. X-ray of skull: calcification in the right frontal region and in the falx.

V.E.G.: normal pressure. Ratio 0.38 (0.36/0.40). 3rd ventricle 4 mm. Normal surface air. Temperature 38.1° C. the same day. No other complications.

Follow-up: was investigated in the R.H. Psychiatric Department at the age of 11 years because of temper tantrums. Re-admitted to N.K. department at the age of 11 years 6 months because of continuing convulsions at intervals of 2-3 weeks and discharge from the right ear. The seizures were usually localised to the jaw muscles. She had temper tantrums, difficulties at school and had for a while been in a special class. E.E.G. showed moderate dysrhythmia over both hemispheres. On examination she appeared dull though normal otherwise and there was no indication for further neurosurgical investigation or treatment. She was discharged to the hospital for epileptics where she stayed for some time. From there she went to a home for chronic epileptics and a residential school from the age of 12 to 22 years. At the age of 20 she was admitted to hospital for biopsy of glands in the neck. Microscopy showed tuberculous structure. Now works as a cleaner in a paediatric department and gets an invalid pension. Admitted to a neurological department at the age of 24 because of dysaesthesia in the left arm. Sequelae of glandular biopsy found with a lesion involving the long thoracic nerve. Otological examination showed a doubtful loss of hearing on the right side and severe reduction on the left side. L.E.G.: dilatation of the anterior horns on both sides. Satisfactory filling of the whole ventricular system and no abnormal surface air found. E.E.G. showed a focus anteriorly in the right hemisphere. Anti-epileptic treatment resumed. The patient appeared rather simple and perhaps slightly mentally retarded.

Diagnosis: epilepsy (? past), total loss of hearing on the right side and decreased hearing on the left, sequelae of tuberculosis, possible intellectual inferiority.

Summary: a girl who had tuberculosis from the age of 18 months and chronic otitis from the age of 2½ years. Seizures first occurred when she was 2 years 4 months. V.E.G. at 5 years showed a ratio of 0.38, 3rd ventricle 4 mm. Seizures continued and she was admitted to a hospital for epileptics and from there to a special home for epileptics from the age of 12 to 22 years. L.E.G. was performed at the age of 24 and showed some dilatation of the anterior horns. She has total loss of hearing on one side and reduced hearing on the other. She appears to be somewhat simple but manages to work.

116.

N.K. no. 01867/48. Boy born 9. 8. 40. No familial predisposition. Only child. Mother had several attacks of influenza during pregnancy and vomited. Forceps delivery because of incorrect head position after 3 days in labour. Birth weight 3800 g. There was much subcutaneous bruising and a left-sided facial paresis.

Symptoms: at the age of one week had occasional facial twitching and transitory neck stiffness. Nothing more noticed until he was 18 months old when he seemed to fall often. At the age of 5 years he had spasmodic jerks down the left side of the body and these occurred on ten occasions. At the age of 6 years he had a fractured skull. Did well at school.

Admitted to N.K. department at the age of 7 years 10 months. Eye examination normal. Head circumference 54 cm. Left leg 2 cm. shorter than the right. Left-sided Babinski and slight left-sided spastic hemiparesis. E.E.G. showed some low frequencies and occasional scattered epileptic changes over the right frontal region.

V.E.G.: pressure 140. Ratio 0.38 (0.39/0.37). 3rd ventricle 7 mm. Temperature 38° C., normal the day after.

Arteriography showed no sign of a tumour.

Follow-up: investigated at the Orthopaedic Hospital at the age of 11 years because of a slight degree of spastic monoparesis and epilepsy. His own doctor (from the Faroe Islands) wrote to say that he was completely fit and mentally normal. The left leg was still somewhat shorter than the right and there was obvious lumbar scoliosis convex to the left. There was also a left-sided equinus deformity. No seizures.

Diagnosis: left-sided spastic hemiplegia.

Summary: a boy whose mother had repeated attacks of influenza during pregnancy and whose delivery was by forceps. There was a left-sided facial paresis. At the age of a week there was facial twitching and at the age of 5 years he had spasmodic jerks down the left side of the body. He sustained a fractured skull at the age of 6 years. V.E.G. when nearly 8 years old showed a ratio of 0.38, 3rd ventricle 7 mm. At follow-up he was said to be mentally normal. He still had a left-sided spastic hemiplegia.

117.

N.K. no. 03308/49. Boy born 13. 12. 47. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3800 g.

Symptoms: jaundiced from the 2nd until the 10th day of life. Retarded in development. Focused at 3 months and sat up at a year. When 3-4 months old had a sudden clonic tonic convulsion during which he became rigid and bent his head back. It lasted 5-15 minutes and was repeated 4-5 times. Admitted to the R.H. Paediatric Department and treated with thyroid hormone for a while. Later admitted for investigation of a possible cerebral tumor. Developmental quotient 65.

Admitted to N.K. department at the age of 15 months. Eye examination revealed rather slit-like eyes, otherwise nothing abnormal. Head circumference 50 cm. Reflexes normal. Retarded both physically and mentally. X-ray of skull showed it to be large with thin cranial walls. Increased digital markings anteriorly. E.E.G. not done. Sub-dural puncture: negative result.

S.E.G.: pressure 500. Ratio 0.38 (0.36/0.39). 3rd ventricle 4 mm. Even distribution of surface air. Temperature 39.1° C. the day after, otherwise no complaints.

Follow-up: admitted to a children's hospital at the age of 2 years suffering from bilateral hydronephrosis, bilateral ureteric dilatation, pyuria, oligophrenia and umbilical hernia. Operated on for the urinary tract disorder. Admitted from the age of 3-5 years to a home for chronic sick and placed under State mental care at the age of 4 years. Developmental quotient on several occasions varied between 58 and 66. Placed in an ordinary school at the age of 8 years but he did not get on at all well so he was transferred to a special boarding-school for the mentally retarded at the age of 9 years. It is thought that he does not understand very much but he can count to 50 and appears a pleasant child. He does not appear to have any endocrine disorder. Head circumference 56 cm. Speech is good. Eye examination showed slight ptosis of the left upper eyelid but no other abnormality. Reflexes normal. Cannot hop on right leg.

Diagnosis: oligophrenia (debilitas mentis), ptosis of the left upper eyelid.

Summary: a boy who was jaundiced from the 2nd to the 10th day of life, and who had always been retarded. Convulsions occurred when 3 months old. S.E.G. at 15 months of age showed a ratio of 0.38, 3rd ventricle 4 mm. He was later operated on for a urinary tract disorder. Placed in a school for mentally retarded. Developmental quotient 66.

118.

N.K. no. 21143/53. Boy born 1. 4. 52. Familial predisposition: a cousin had convulsions at the age of 6-7 years. Pregnancy normal. Birth 7 weeks premature and somewhat precipitate. Birth weight 3000 g. Was immediately cyanotic and had severe bleeding from the umbilicus.

Symptoms: at the age of 6 months it became obvious that development was not normal. He could not sit and constantly shook his head. At the age of 11 months, in connection with fever he had jerks in all four extremities. At the age of 13 months he had an episode of unconsciousness and cyanosis and jerks down the left side. Admitted to hospital and transferred to the R.H. Paediatric Department at the age of 14 months.

Re-admitted a month later after a 30-minute episode of unconsciousness. L.E.G. showed increased surface air. E.E.G. normal. X-ray of skull normal. Developmental quotient 42.

Admitted to N.K. department at the age of 16 months. Eye examination: slight divergent squint. Head circumference 42 cm. Could sit alone and stand with support. Reflexes brisk. Bilateral Babinski.

V.E.G.: pressure 20. Ratio 0.38 (0.39/0.38). 3rd ventricle 4 mm. Slight increase of surface air, mostly to the front. Temperature 38.9° C. the same day, normal on the 3rd day. No complaints otherwise.

Follow-up: placed under State mental care at home when 4 years old. Admitted on two occasions to a children's hospital, the last time when aged 3 years. Had a chronic kidney disease and rachitic changes in the diaphyses together with dwarfism. An attempt to perform L.E.G. was unsuccessful. E.E.G. showed severe diffuse dysrhythmia but nothing focal. Developmental quotient at the age of 3 years was 48. Physical examination: had made progress. Talked quite a lot but could only be understood by those who knew him. Was very anxious. Walked well and used his hands well. Head circumference 47 cm. Eye examination normal. Patellar reflexes elicited over the whole tibial area. Bilateral ankle clonus. Left-sided Babinski and doubtful right-sided Babinski. Brisk tendon reflexes in both arms.

Diagnosis: oligophrenia (imbecility), microcephaly.

Summary: a boy with a family history of convulsions and whose birth was said to be 7 weeks premature. Cyanosis present at birth. From the age of 6 months retarded development noticed. Seizures occurred at 11 months and V.E.G. at 16 months showed a ratio of 0.38, 3rd ventricle 4 mm. Placed under State mental care at home. He has a chronic kidney complaint and possible rickets with dwarfism.

119.

N.K. no. 3946/43. Boy born 27.9.35. No familial predisposition. Pregnancy: was ill the whole time and often tired. No albuminuria or hypertension. Birth normal. Birth weight 4500 g.

Symptoms: 2 years before admission he fell and hit the back of his head on a kerbstone. Was dizzy and vomited. Following this he had pneumonia and apurulent poliomyelitis with meningeal reaction. Was admitted to a hospital for infectious diseases. Ten weeks before admission he hit his head on a stone. He was treated in a casualty department but became ill on the way home and was admitted to hospital. A depressed fracture in the left fronto-parietal region was found. During his stay in hospital he caught scarlet fever and was again admitted to a hospital for infectious diseases.

Admitted to N.K. department at the age of 7 years 6 months. On the left side of the forehead was a 4 × 3 cm. wide and 1 cm. deep depression. Eye examination, reflexes and intelligence normal. X-ray of skull showed a large defect in the left parietal region.

V.E.G.: pressure 155. Ratio 0.39 (0.41/0.37). 3rd ventricle 5 mm. Temperature 38.6° C. the same day, normal on the 4th day. No other complaints.

Follow-up: seen as an out-patient at the age of 9 years when all was well. At the age of 19 he complained of slight dizziness on effort and E.E.G. was slightly abnormal. X-ray of skull showed no abnormality apart from the sequelae of the skull fracture. He has since been well and works in his father's shop. During military service he was admitted to hospital because of a nervous breakdown but he succeeded in completing his service. He never has headaches. Physical examination: normal, healthy appearance. Head circumference 58 cm. Small scar on the left temple. Eye examination and reflexes normal. Chest slightly funnel-shaped.

Diagnosis: healthy.

Summary: a boy who sustained a head injury at the age of 5 years and this was followed by pneumonia and apurulent poliomyelitis. At the age of 7 years he again injured his head and a skull fracture was revealed on X-ray. V.E.G. ratio was 0.39, 3rd ventricle 5 mm. At follow-up he had been perfectly well and had completed his military service.

120.

N.K. no. 02169a/48. Boy born 22. 1. 48. No familial predisposition. Fourth of four children. Pregnancy normal. Birth 6 weeks premature. No asphyxia. Birth weight 2700 g.

Symptoms: generalised rigidity since birth. Trembled periodically and always very restless. At the age of 4 months had a sore throat and temperature of 40.5° C. Admitted to the R.H. Paediatric Department because of poor weight gain. Sub-dural puncture: on the left side no abnormality; on the right slightly yellow-coloured fluid. Eyes normal. X-ray of skull normal.

First admitted to N.K. department at the age of 4 months. Neck stiffness present together with "cracked pot" sound on cranial percussion. Head circumference 42 cm. Eye examination normal. Did not seem to hear and cried a great deal on being touched. Considerable increase of muscle tone particularly in the right leg.

V.E.G.: pressure 150. Ratio 0.39 (0.38/0.39). 3rd ventricle ? Normal cortical air. Temperature 38° C. the day after examination which persisted until the 6th day. Otherwise no complaints. Repeated V.E.G. 14 days later showed a ratio of 0.39 (0.37/0.42). 3rd ventricle 4 mm. No post-operative complaints.

Second admission to N.K. department 2 months later. Had been very restless and miserable. Had increasing left-sided jerks.

V.E.G.: normal pressure, clear fluid. Ratio 0.39 (0.37/0.42). 3rd ventricle 4 mm. Temperature 38.6° C. the same day, otherwise no complaints.

Follow-up: died in hospital at the age of 7 months. Diagnosis: diffuse cerebral atrophy, pneumonia. On admission he was rigid with a tendency to opisthotonus. Rigidity varied a great deal but was more pronounced in the arms. Two days before he died he developed a high fever and pneumonia. No autopsy was performed.

Diagnosis: rigidity, oligophrenia (? degree), epilepsy.

Summary: a boy who had been rigid since birth. V.E.G. at 4 months showed a ratio of 0.39. Repeat V.E.G. at 6 months showed a ratio of 0.39, 3rd ventricle 4 mm. He died at 7 months from pneumonia with high fever.

121.

N.K. no. 02146/48. Boy born 27. 3. 47. No information on familial predisposition. Third of three children. Pregnancy: hypertension and eclampsia. Birth two weeks premature. Birth weight 2100 g.

Symptoms: gastro-enteritis from first days of life and remained in hospital for 3½ months. At about 10 months of age it was noticed that the patient was somewhat retarded. The left arm was paralysed and he did not want to use the left hand. He could not sit up. The mental development appeared almost normal and there had been improvement prior to admission. Admitted to a paediatric department for observation.

Admitted to N.K. department at the age of 16 months. Eye examination: convergent squint, otherwise no abnormality. Left arm very flaccid and paralysed. Left-sided Babinski. X-ray of skull normal. E.E.G. not done.

S.E.G.: pressure 300. Ratio 0.39 (0.37/0.42). 3rd ventricle 11 mm. Burr holes were made in both frontal regions. Clear fluid was found on both sides with thickened arachnoid tissue. The patient could not be roused after the examination, in spite of stimulants, except for a short time the following morning and he died immediately afterwards. Brain autopsy showed moderate ventricular dilatation but no focal processes. The contours did not appear entirely normal but this was possibly due to hyperaemia. Autopsy provided no explanation of the cause of death. Microscopy showed severe hyperaemia.

Diagnosis: left hemiplegia, ? mental state.

Summary: a boy who was born two weeks prematurely after a pregnancy complicated by hypertension and eclampsia. Suffered from gastro-enteritis from first days of life and at about 10 months of age it was noticed that development was retarded and he did not use his left hand. S.E.G. at 16 months showed a ratio 0.39, 3rd ventricle 11 mm. Burr holes were made and death followed the next morning after only a short period of consciousness.

122.

N.K. no. 03098/49. Boy born 17. 6. 48. Familial predisposition: cousin died at 2 years of age from convulsions and hydrocephalus. Another cousin was feeble-minded and died at 10 months. Fourth of four children. Pregnancy normal. Birth was easy though injections were given. Birth weight 4450 g.

Symptoms: very rigid since birth. At the age of two months he had gastro-enteritis and convulsions and was admitted to hospital for investigation of a possible sub-dural haematoma. Development poor. Appeared imbecile. Admitted to a paediatric department because of convulsions.

Admitted to N.K. department at the age of 7 months. Eye examination normal. Head circumference 47.5 cm. "Cracked pot" sound on cranial percussion. Mental development very reduced. Reflexes normal.

S.E.G.: ratio 0.39 (0.39/0.39). 3rd ventricle 2 mm. Increased surface air on the right side anteriorly corresponding to the Sylvian fissure. Temperature 38.8° C. the day after, otherwise no complaints.

Follow-up: his condition deteriorated and he was admitted on 4 occasions to a paediatric department, the last time at the age of 13 months when he died. He had had increasing convulsions, temperature to 41° C. and general deterioration. X-ray showed pulmonary infiltration. Autopsy: sub-chronic haematoma in the right anterior cranial fossa. Epidural haematoma. Right-sided bronchopneumonia and purulent bronchitis. Brain examination revealed severe oedema of the meninges.

Diagnosis: rigidity, epilepsy, oligophrenia (? imbecile), sub-chronic haematoma in the right anterior cranial fossa, epidural haematoma.

Summary: a boy with a family history of feeble-mindedness. He was rigid from birth and development was poor. Convulsions occurred at the age of two months. S.E.G. at 7 months showed a ratio of 0.39, 3rd ventricle 2 mm. with increased surface air. His condition steadily deteriorated and he died at the age of 13 months.

123.

N.K. no. 07292/51. Boy born 6. 4. 45. Familial predisposition: mother's brother and patient's brother had convulsions. Third of four children. Pregnancy normal. Birth uncomplicated but the patient was given a number of injections. Birth weight 3500-4000 g.

Symptoms: walked at 3 years. Intellectual ability rather reduced. From the age of 4½ years he had increasingly frequent convulsions with loss of consciousness. The child was first taken to a doctor at the age of 6 years because the parents thought he was somewhat retarded and had a large head. At that time he could not feed himself and was not toilet-trained. Admitted to the R.H. Paediatric Department at the age of 6 years. E.E.G.: very irregular curves, presumably abnormal.

Admitted to N.K. department at 6 years. Head circumference 56 cm. Eye examination normal. Patellar reflexes brisk.

S.E.G.: pressure 320. Clear fluid. Ratio 0.39 (0.39/0.39). 3rd ventricle 8 mm. Normal surface air. Temperature 38° C. the same day, otherwise no complaints.

Follow-up: in a State mental institution from the age of 6 years 4 months. Diagnosed as a case of idiocy, cerebral atrophy, epilepsy and hydrocephalus. The patient is described as being of very low-grade intelligence, without speech or understanding of speech and completely disinterested in his surroundings. He has occasional convulsions. On physical examination he was well-developed. Head circumference 55.4 cm. No reflex changes. Gait slow, broad-based and unsteady. Eye movements normal. Has habit movements of both hands.

Diagnosis: oligophrenia (idiocy), epilepsy.

Summary: a boy with a family history of convulsions. Late in development and from the age of 4½ had an increasing number of convulsions. S.E.G. at 6 years showed a ratio of 0.39, 3rd ventricle 8 mm. Is under State mental care and is a low-grade idiot with periodic seizures.

124.

N.K. no. 09521/52. Boy born 8.9.51. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: admitted to hospital at the age of 4 months because of myoclonic jerks in the left hand and signs of rickets were found. Convulsions increased and grew worse after whooping-cough. Again admitted to hospital and thence to the R.H. Paediatric Department. Seizures characterised by jerks in the left arm and both legs. E.E.G. showed focal dysrhythmia in the right occipital region. X-ray of skull normal. Eye examination revealed the patient to be blind and presumably also deaf.

Admitted to N.K. department at the age of 11 months. Eye examination: ? blindness. Head circumference 47.5 cm. It was not possible to make any contact with the patient and he did not react to light or sound. Bilateral Babinski. Could not raise his head.

S.E.G.: pressure 200, clear fluid. The ventricular system appeared moderately dilated. No definitely measurable pictures were obtained because the right cranial wall was missing on the A-P picture. By using other pictures the ratio was calculated to be 0.39 (0.40?(0.37), 3rd ventricle 14 mm. No rise in temperature or complications after the examination.

Follow-up: admitted to hospital for epileptics at the age of 3 years 10 months. Has had only one convulsion in about a year. Has begun to walk but cannot talk and is not toilet-trained. Is of very low intelligence. Takes phenobarbitone for his occasional convulsions. Physical examination: appears severely mentally retarded. Head circumference 50.5 cm. No abnormal eye signs. Left-sided Babinski and doubtful right-sided Babinski. No ankle clonus. Patellar reflexes brisk.

Diagnosis: oligophrenia (idiocy), epilepsy, slight neurological changes in the legs.

Summary: a boy who had convulsions from the age of 4 months involving the left hand and later both legs and was mentally retarded with presumably no vision or hearing. S.E.G. at 11 months showed a ratio of 0.39. 3rd ventricle 14 mm. Is in a hospital for epileptics. Is extremely mentally retarded but has only occasional seizures.

125.

N.K. no. 21891/54. Boy born 9.3.53. Familial predisposition: parents distantly related. Mother's cousin schizophrenic. Only child. Pregnancy: was ill the whole time with vomiting and loss of weight. Delivery normal. Birth weight 3500 g.

Symptoms: when the patient was 2-3 months old it was noticed that he could not see. Admitted to the R.H. Paediatric Department at the age of 5 months. Amblyopia of unknown origin and nystagmus were found. E.E.G. showed no definite abnormality.

Admitted to N.K. department at the age of a year. Eye examination: blindness and hypermetropia, ? retarded myelogenesis. Probably could not see. Eyes constantly moving. Head circumference 48 cm. Appeared frightened. Could stand but not walk. Reflexes not definitely abnormal. E.E.G. and skull X-ray normal.

V.E.G.: pressure 200. Ratio 0.39 (0.36/0.41). 3rd ventricle 13 mm. Increased surface air. Temperature 38.6° C. the same day and still raised the next day. Otherwise no complaints. Microscopy of cortex showed normal conditions.

Follow-up: seen in the R.H. Paediatric Department at the age of a year. Understanding thought to correspond to age but still says nothing. Referred to the Blind Institute. Has been fit and well and never has febrile episodes. Speech is normal and understanding good. He is toilet-trained. Physically well-developed. Possibly sees light as sunlight appears to bother him. Walked alone at the age of 2 years. Did not talk until 2½ but distinctly from the beginning. Is very musical. Physical examination: head circumference 51.5 cm. Eye movements full. Perception of light but probably no definite sight. Reflexes normal. All movements free and well co-ordinated.

Diagnosis: blindness.

Summary: a child whose parents are distantly related. The mother was ill during the whole pregnancy. At the age of 2-3 months it was noticed that he could not see. V.E.G. at one year showed a ratio 0.39, 3rd ventricle 13 mm. He reacts to strong light but is presumably blind. Healthy otherwise.

126.

N.K. no. 07812/51. Boy born 15. 1. 50. No familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight 3100 g.

Symptoms: at the age of about 18 months fell out of bed. No immediate after-effects. Later had sore throat, diarrhoea and fever. On the day of admission to hospital had generalised convulsions. Unconscious on admission with neck and back stiffness. Lumbar puncture normal. Left-sided convulsions followed.

Admitted to N.K. department at the age of 20 months. Eye examination: right pupil larger than the left. Pupil reaction slower on the left. Was sleepy and resistant to examination. Doubtful left-sided Babinski. Marked rigidity of left-sided extremities present. Head circumference normal. E.E.G.: clear side difference with highest number of low frequencies over the right hemisphere posteriorly.

S.E.G.: pressure 250, clear fluid. Ratio 0.40 (0.40/0.40). 3rd ventricle 5 mm. Temperature 38° C. the day after the examination. Otherwise no complaints.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. E.E.G.: no definite abnormality seen. Is a good and contented child who understands well. Speech limited to single words though he is about 6 years old. Uses his right hand more than his left and there is obvious equinus deformity of the left foot. Is under State mental care at home. Investigated at the Orthopaedic Hospital's cerebral palsy clinic at the age of 8 years 3 months: ? post-encephalitic encephalopathia. Atypical cerebral palsy (mixed pyramidal and striate type, predominantly left-sided tetraplegia). Debilitas mentis with aphasia. Symptomatic epilepsy. Post-encephalitic behaviour disturbance.

Diagnosis: left-sided hemiplegia (tetraplegia), epilepsy, oligophrenia (debilitas mentis).

Summary: a boy who at the age of 18 months sustained a head injury and a febrile disorder followed with convulsions and loss of consciousness. S.E.G. at that time showed a ratio of 0.40, 3rd ventricle 5 mm. He is now under State mental care at home. He has an atypical cerebral palsy with a predominating left-sided tetraplegia.

127.

N.K. no. 23150/55. Girl born 17. 2. 55. No relevant familial predisposition. Second of two children. Pregnancy: nausea, vomiting and dizziness most of the time. Birth 5-6 weeks premature, breech presentation, no asphyxia. Birth weight 1900 g.

Symptoms: was jaundiced for about a month. Was flaccid and frequently had to be tube-fed. In hospital skull X-ray was highly suspicious of increased circumference.

Admitted to N.K. department at the age of a month. Eye examination normal. Lay in slight opisthotonus position. Head circumference 35.5 cm. Other examinations showed no abnormality. X-ray of skull normal. E.E.G. not done. Sub-dural puncture showed clear fluid on both sides.

V.E.G.: pressure 100, clear fluid. There were no really satisfactory A-P pictures but on the temporal horn pictures there was equal dilatation on both sides. Ratio was 0.40, 3rd ventricle 6 mm. No complaints following the examination.

Follow-up: sat up at 6 months and walked at 14 months. Says single words. Has never crawled and has no involuntary movements. Now and then can be a little withdrawn. Physical examination: normal, healthy appearance. Head circumference 46.2 cm. Speech corresponds to age. Eye examination and reflexes normal. Hand movements normal. Gait is a little cautious but corresponds to age.

Diagnosis: healthy.

Summary: girl whose mother had a pregnancy complicated by vomiting. Birth was by breech presentation and 5-6 weeks premature. She was jaundiced for a month and because of some flaccidity and the possibility of an increased head circumference V.E.G. was carried out at one month. Ratio was 0.40, 3rd ventricle 6 mm. Since then she has developed normally and physical examination showed no abnormality.

128.

N.K. no. 01485/48. Girl born 20. 2. 47. No known familial predisposition. Fifth of five children. Pregnancy normal. Delivery difficult and rather prolonged. Birth weight 3600 g.

Symptoms: since the age of two months had seizures during which the left arm jerked and was extended. Lasted from a few seconds to a couple of minutes and the eyes turned to the left. Gradually developed into generalised seizures occurring as many as 8 times daily. Admitted to the R.H. Paediatric Department at just over a year. X-ray of skull normal. I.Q. 43. Head circumference 43 cm.

Admitted to N.K. department at 13 months. Eye examination normal. Could not focus and face was expressionless. Right-sided Babinski, doubtful left-sided Babinski. Burr holes showed no sub-dural hygroma.

V.E.G: pressure 30. There appeared to be a septum pellucidum cyst. It was not possible to make an exact ratio measurement but a provisional estimate was 0.41 (0.41/0.41), 3rd ventricle 4 mm? Temperature 38.4° C. the day after, otherwise no complaints.

Follow-up: seen in the R.H. Paediatric Department at the age of 2 years and placed under State mental care. Head circumference 47 cm. Oligophrenic, characterised by lacking cortical function. Developmental quotient 19. Admitted to a State mental institution at the age of 4 years. Diagnosed as a case of oligophrenia (idiot), tetraplegia, previous epilepsy and petit mal. During admission it was not possible to perform any assessment of intelligence. She appeared completely vacant and out of contact with her surroundings. She could sit up but not support herself. Had 20° contractures of the knees and performed frequent small athetoid arm and finger movements. L.E.G. at the age of 7 years 8 months: there was bleeding and convulsions in connection with the examination. Diffuse dilatation of the ventricular system was present. 3rd ventricle elongated and there was presumably a septum cyst. The ratio could not be measured but the left side was more dilated than the right and the angles were more rounded. During the past 3-4 months there had been a total of 10 generalised convulsions and daily episodes of petit mal. Physical examination: head circumference 47.8 cm. Impossible to make any contact with the child. All reflexes very brisk. Bilateral Babinski. No definite ankle or patellar clonus. No certain contracture but spontaneously holds the knee-joints slightly flexed. Eyes normal.

Diagnosis: oligophrenia (idiocy), epilepsy, possible spastic tetraplegia.

Summary: a girl whose delivery was prolonged. Seizures began at two months, first on the left side and later generalised. Mental development was retarded. V.E.G. at 13 months showed a possible septum pellucidum cyst. Ratio 0.41. Placed under State mental care. Developmental quotient 19. Severely mentally retarded, impossible to make any contact with and still having seizures.

129.

N.K. no. 02986a/49. Boy born 1.8.45. No relevant familial predisposition. Only child. Pregnancy: mother had a severe shock in the 6th month. Delivery said to be normal. Birth weight 3150 g.

Symptoms: admitted to a paediatric department at age of 3 days because of intracranial haemorrhage and neonatal jaundice. Spinal fluid was bloodstained. Admitted for 6 weeks and symptom-free thereafter. At the age of two years had a generalised convulsion and loss of consciousness. Admitted to a paediatric department.

Admitted to N.K. department at the age of 3 years. Appeared mentally retarded. Eye examination: no definite abnormality. Head circumference 54 cm. "Cracked pot" sound on cranial percussion. Reflexes normal. X-ray of skull showed it to be large with a deep posterior fossa.

V.E.G: pressure 40. Ratio 0.41 (0.42/0.39), 3rd ventricle 5 mm. Temperature 39° C. the same day, otherwise no complaints.

Re-admitted to N.K. department 3 months later for observation.

S.E.G: pressure 320, clear fluid. Ratio 0.41 (0.41/0.40). 3rd ventricle 5 mm. Burr hole made over the right post-central region. Cortex appeared normal. Microscopy showed slightly oedematous sub-cortical tissue. Temperature 38.1° C. the same day, otherwise no complaints.

Follow-up: attends a special school. Has had no seizures since the age of two years. Talks well. Operated on for hernia but otherwise no illnesses. Walked at 3 years and was altogether rather slow in development. Physical examination: appears healthy. Reflexes

says only single words and there is no understanding of speech. He grinds his teeth and dribbles. Head circumference 53.5 cm. Divergent squint present. He can only walk with strong support. There is a "four-finger line" in the left hand.

Diagnosis: oligophrenia (? idiocy).

Summary: a boy whose mother appeared somewhat retarded. Severely asphyxiated at birth. Retarded development noticed from the age of 8-9 months. V.E.G. at 9 months showed a ratio of 0.43, 3rd ventricle 3 mm. At follow-up he was severely retarded and should be under State mental care but this is not the parent's wish at present.

134.

N.K. no. 06242 a/50. Boy born 3.6.49. No familial predisposition. Fourth of four children. Pregnancy: nephropathy and hypertension treated medically. Forceps delivery because of intra-uterine asphyxia. Birth weight 3200 g.

Symptoms: immediately placed in incubator. Head in opisthotonus position and a single episode of one-sided change of colour. Subdural puncture: hygroma on the left side.

Admitted to N.K. department at the age of two months. Head circumference 38 cm. "Cracked pot" sound on cranial percussion. Restless and much head movement. Doubtful Babinski. Sub-dural puncture: clear fluid on the left side and a drop of slightly blood-stained fluid on the right.

V.E.G.: pressure 50. Ratio 0.43 (0.44/0.43). 3rd ventricle 6 mm. No complaints after the examination.

Re-admitted to N.K. department at 15 months. Had been fairly well and had made some progress. Sat alone at the age of a year and began to say single words. I.Q. 50. Moved right side more than the left. Often cried. Physical examination: eyes normal. Head circumference 46 cm. Doubtful bilateral Babinski.

S.E.G.: pressure 250. Pictures rather indistinct. Ratio 0.38 (0.39/0.37). 3rd ventricle 8 mm. No complaints after the examination.

Follow-up: admitted to State mental institution at the age of 2 years 8 months. Diagnosed as a case of imbecility. During admission he had almost chronic ear discharge and was treated in different otological departments, by left-sided radical operation amongst other methods of treatment. He has a very low intelligence and is completely incontinent and helpless. No seizures. Physical examination: very retarded. Can sit alone for a short while. Understands nothing and says nothing. No seizures. Eyes normal. Head circumference 46.8 cm. Reflexes normal.

Diagnosis: oligophrenia (? idiocy, ? imbecility), microcephaly.

Summary: a boy whose mother had a kidney disorder during pregnancy. Delivery was difficult. There was intra uterine asphyxia and the child was immediately put into an incubator. V.E.G. at two months showed a ratio of 0.43, 3rd ventricle 6 mm. S.E.G. at 15 months showed a ratio of 0.38, 3rd ventricle 8 mm. He is in a State mental institution, has very low intelligence and is completely helpless.

135.

N.K. no. 05217/50. Boy born 6.2.49. No familial predisposition. Fifth of five children. Pregnancy normal. Delivery 3 weeks premature, membranes ruptured 36 hours beforehand and birth was medically induced. Lasted 3 hours. There was asphyxia and flaccidity. Birth weight 3750 g.

Symptoms: blue and flaccid for the first few days and the right arm was paralysed. Right foot turned inwards. Severe jaundice was present and he would not suck. Poor weight-gain at first. Slow in development, particularly in the motor system. Admitted to the R.H. Paediatric Department at the age of a year. X-ray showed possible hydrocephalus. L.E.G.: severe dilatation of both lateral ventricles. Ratio 0.44 (0.44/0.45). 3rd ventricle 9 mm. Increased cortical air frontally.

Admitted to N.K. department at 13 months. Head circumference 51 cm. "Cracked pot" sound on cranial percussion. Eyes normal. Legs rather flaccid but brisk patellar reflexes present. No Babinski. E.E.G. not definitely abnormal. Nothing further to add to the previous P.E.G.

Follow-up: admitted to State mental institution at the age of 2 years 9 months. Diagnosed as a case of idiocy and albuminuria. Developmental quotient assessed many times from the age of a year when it was 63, falling 18 months later to 48. Head circumference then 55 cm. No spasticity. On admission to another State mental institution at the age of 5 years the temperature rose from 37.9°C . to 40.2°C . He suddenly became very ill and the temperature rose further to 41.7°C . He became shocked and quickly died. Autopsy showed no signs of pneumonia. Autopsy diagnosis: normal findings. Special microscopy showed hyperaemic liver tissue and kidney tissue with glomerular changes. Brain autopsy: severe cerebral oedema and congenital cerebral dysplasia; slight hydrocephalus and megaloccephaly.

Diagnosis: oligophrenia (idiocy), chronic kidney disease with albuminuria, ? cerebral hyperpyrexia.

Summary: boy who was severely asphyxiated and flaccid at birth. He was jaundiced and in a poor general condition neonatally. L.E.G. at a year showed a ratio of 0.44, 3rd ventricle 9 mm. and increased cortical air. Placed in a State mental institution and on being transferred to another developed hyperpyrexia and died.

136.

N.K. no. 22380/54. Girl born 18.9.53. No familial predisposition. Only child. Pregnancy normal. Birth difficult and lasted three days. Birth weight 3500 g.

Symptoms: convulsions occurred a few hours after birth and lasted for 3 days. At 6 months left-sided, later also right-sided convulsions occurred. Admitted to the R.H. Paediatric Department at 10 months. Developmental quotient 58. E.E.G. severely abnormal. L.E.G. showed an atrophic lesion of mixed type.

Admitted to N.K. department at 11 months. Eye examination: alternating divergent squint. Head circumference 42 cm. Asymmetry of forehead and right side of the face. Reflexes normal.

V.E.G.: pressure 150, clear fluid. Ratio 0.44 (0.42/0.46). 3rd ventricle 6 mm. Increased surface air, especially frontally. Small Verga cyst seen. Temperature 37.8°C . the day after. Otherwise no complaints.

Follow-up: Admitted to State mental institution at the age of a year. Has been in status epilepticus many times but has had no convulsions during the past year. Physical examination: appears considerably retarded. Head circumference 44.5 cm. No eye changes. Says single words. Patellar reflexes brisk, no ankle clonus. Doubtful bilateral Babinski. Can walk and stand alone.

Diagnosis: oligophrenia (? debilitas mentis, ? imbecility), epilepsy, microcephaly.

Summary: a girl whose delivery was difficult and who had convulsions almost from birth. Development was retarded. V.E.G. at 11 months showed a ratio of 0.44, 3rd ventricle 6 mm., increased surface air. Is in hospital under State mental care, is microcephalic and severely mentally retarded.

137.

N.K. no. 24030/55. Boy born 21.2.54. No familial predisposition. Only child. Pregnancy and delivery normal but child did not cry immediately and was asphyxiated. Birth weight 4200 g.

Symptoms: immediately after birth there was trembling, a cerebral cry and opisthotonus, and on the second day of life repeated convulsions. Admitted to hospital and at 3 weeks transferred to the R.H. Paediatric Department. At that time he was rigid in all extremities. E.E.G. was normal as was sub-dural puncture. Re-admitted at the age of 14 months. E.E.G. showed a very abnormal curve. L.E.G. showed increased air on surface corresponding to the frontal lobes. Ventricular filling incomplete.

Admitted to N.K. department at 14 months. Constant nystagmus. Pronounced spastic tetraplegia. Completely disinterested in surroundings. X-ray of skull normal.

V.E.G.: pressure 100. Cortex appeared very atrophic. Ratio 0.44 (0.43/0.45). 3rd ventricle 14 mm. Severe cortical atrophy with large air collections. Temperature 39.4°C . after the examination.

Right-sided arteriography: probably severe cortical atrophy with sub-arachnoid communicating air collections. Burr hole: the arachnoid was raised up by a large fluid collection. Cortex atrophic. On the medial side of the hemisphere there was a large fluid cyst, undoubtedly communicating with the sub-arachnoid space. Microscopy showed cortex with chronic ganglion cell degeneration. Temperature 38.8° C. after examination.

Follow-up: under State mental care in a special nursery home at the age of a year and nine months. Was feverish and ill during most of his stay there. Had pronounced difficulty in swallowing and died at the age of 2 years 2 months in high fever. Death certificate diagnosis: hyperpyrexia, atrophic encephalopathy. No autopsy performed.

Diagnosis: spastic tetraplegia, oligophrenia (idiocy), epilepsy.

Summary: a boy who was asphyxiated at birth and developed cerebral symptoms immediately afterwards. V.E.G. at 14 months showed a ratio of 0.44, 3rd ventricle 14 mm. and severe atrophy which was later verified by burr hole. Placed under State mental care and died in a nursery home in hyperpyrexia at the age of two years two months.

138.

N.K. no. 22298/54. Boy born 4. 1. 52. No familial predisposition. Only child. Pregnancy normal. Birth induced, otherwise normal. Birth weight 4100 g.

Symptoms: congenital foot deformity treated with splints and arch supports at the Orthopaedic Hospital. From the age of two years he had episodes of crying and shaking his head, occurring up to four times a day and lasting 15–20 minutes. The episodes were accompanied by vomiting. No convulsions. He had developed fairly well, understood everything but at the time of admission did not talk. Admitted to the R.H. Paediatric Department at the age of 2½ years. L.E.G. ratio 0.44 (0.43/0.44). 3rd ventricle 10 mm. Increased cerebellar air present. E.E.G. and skull X-ray normal. Developmental quotient 55.

Admitted to N.K. department at 2½ years. Slight convergent squint. Head circumference 44.5 cm. Bilateral pes planus and pes valgus deformity with broad-based gait. E.E.G. normal.

V.E.G: pressure 150. Ratio 0.45 (0.42/0.47). 3rd ventricle 7 mm. Increased subdural air. Temperature 37.8° C. the day after, otherwise no abnormality. A non-communicating septum pellucidum cyst was present.

Follow-up: followed up at the Orthopaedic Hospital's cerebral palsy clinic at yearly intervals and also attends the Speech Institute. Has had no seizures since the age of 2½ years. Walks with some difficulty, broad-based and almost ataxic. Hearing good. Vision possibly reduced. Head circumference 56.5 cm. Eyes normal. Reflexes brisk in the arms. Doubtful ankle clonus and Babinski on both sides. Patellar reflexes brisk and elicited over the entire tibia. He says single words and though his mental development does not correspond to his age, he does not appear very retarded. The speech difficulty is the essential problem.

Diagnosis: ataxia ? spastic tetraplegia, aphasia, oligophrenia (? debilitas mentis).

Summary: a boy with a congenital foot deformity who from the age of two years had episodes of crying, possible headache and vomiting. V.E.G. at 2½ showed a ratio of 0.45, 3rd ventricle 7 mm. There was a non-communicating cyst in the septum pellucidum. At follow-up he had become more ataxic, vision was possibly reduced and there was some aphasia and reduction of intellectual ability.

139.

N.K. no. 20809/53. Boy born 8. 8. 52. No familial predisposition. Only child. Pregnancy normal. Birth medically induced, otherwise normal. Birth weight 3450 g.

Symptoms: would not take the breast at all. From the second day of life had trembling involving the whole body. This lasted a month and was followed by convulsions involving the arms. Was admitted to hospital from 1–3 months of age and after discharge had generalised convulsions up to 3 times a day. Admitted to the R.H. Paediatric Department at 4 months with spastic tetraplegia and generalised tonic convulsions. Re-admitted at the age of 8 months with 5–6 seizures daily. E.E.G. and skull X-ray normal.

Admitted to N.K. department at 9 months of age. Gave the impression of being dull

and imbecile. Head circumference 45 cm. Head flattened from one side to the other. Eyes: retinal degeneration of unknown type and nystagmus. Spastic tetraplegia involving the legs more than the arms. Bilateral Babinski. E.E.G.: low frequency activity with high amplitude, highest over the right hemisphere.

S.E.G.: pressure 100, clear fluid. Ratio 0.41 (0.41/0.41). 3rd ventricle 13 mm. Filling not entirely satisfactory. No complaints after the examination.

V.E.G.: (10 days later). Pressure 120. Ratio 0.46 (0.46/0.45). 3rd ventricle 14 mm. Temperature 37.8° C. the day after, otherwise no complications.

Follow-up: admitted to a State mental institution at 18 months of age and diagnosed as an idiot. On admission head circumference was 46 cm. and there was no facial expression. Development was at a complete standstill. He was febrile for 3 days but no abnormality was found on examination of the lungs. He was given antibiotics but died suddenly 12 days after admission. There had been no signs of meningeal reaction and after autopsy it was concluded that he died from influenza of which there was an epidemic in the department at the time. Autopsy diagnosis: microcephaly with macro- and microgyri, progressive cerebral polio- and leucodystrophy following cerebral anoxia.

Diagnosis: spastic tetraplegia, oligophrenia (idiocy), epilepsy, microcephaly.

Summary: a boy who from the second day of life had trembling involving the whole body, and from 4 weeks increasingly frequent convulsions. Signs of a spastic tetraplegia also developed. V.E.G. at 9 months showed a ratio of 0.46, 3rd ventricle 14 mm. He was placed in a State mental institution at 18 months of age and died after three days' high fever of unknown cause.

140.

N.K. no. 22530/54. Boy born 31. 7. 48. No familial predisposition. Pregnancy normal. Birth difficult and prolonged. No asphyxia. Birth weight 4000 g.

Symptoms: always retarded in motor development. First sat alone at the age of a year. Head said to be too large since birth. At 6 months he had convulsions of one minute's duration involving the arms followed by similar episodes at decreasing intervals. Admitted to R.H. Paediatric Department at the age of two years. Diagnosed as possible congenital amyotonia. Re-admitted a year later. Diagnosed as atrophic encephalopathy, oligophrenia, ? imbecility, symptomatic epilepsy. E.E.G. showed severe diffuse dysrhythmia. L.E.G. ratio 0.42 (0.42/0.42). 3rd ventricle 12 mm. Normal surface air.

Admitted to N.K. department at the age of 6 years 2 months. Eye examination normal. X-ray of skull: pronounced venous grooves, particularly frontally on the left side. E.E.G. severely abnormal with low frequency activity.

V.E.G.: pressure 160, clear fluid. Ratio 0.47 (0.45/0.49). 3rd ventricle 13 mm. Temperature 38.4° C. the same day, normal the next day. Otherwise no complications.

Follow-up: is at home and extremely sick. Does not recognise parents. Does not understand what is said to him. Hearing is presumably poor and sight also. Cannot perform spontaneous movements apart from small arm movements. Often has febrile episodes with continuing convulsions at intervals of days to weeks. It is the mother's impression that the disorder continues to progress and she is fully aware of the poor prognosis. On physical examination he was a very sick child but extremely well cared for. Head circumference 54.2 cm. It is not possible to be sure whether he hears or sees anything. Reflexes weak in the arms but slightly increased in the legs with bilateral Babinski. Nystagmus is present.

Diagnosis: progressive neurological disorder, oligophrenia (idiocy), epilepsy.

Summary: boy whose delivery was difficult. Was always physically retarded. Convulsions began at 6 months and increased in frequency. Mental development was very poor. L.E.G. at 2 years showed a ratio of 0.42. V.E.G. at 6 years showed a ratio of 0.47, 3rd ventricle 13 mm. He is severely retarded and has presumably no sight or hearing.

141.

N.K. no. 07475 a/51. Boy born 24. 4. 46. No familial predisposition. First of two children. Pregnancy normal. Birth: breech presentation and 6 weeks premature. Pronounced jaundice which lasted a long time. Birth weight 2000 g.

Symptoms: immediately admitted to hospital because of jaundice. Mental and physical development retarded. At the age of 4 years his gait was unstable and he could say only single words. The night before admission protrusions on both sides of the head were noticed.

Admitted to N.K. department at 4 years 4 months: there was a hand's breadth's protrusion over the left parietal area. It was fluctuant and on puncture was found to be a large haematoma. Mentally he was severely retarded.

Second admission to N.K. department at the age of 5 years 2 months. Continued slow development and could only walk with support. During the 8 days prior to admission there was vomiting and temperature to 38°C . together with change of colour in the face. Physical examination: feeble-minded. Eyes normal. Head large and triangular. X-ray of skull: high cranium with somewhat deep posterior fossa. Coronal suture still open.

S.E.G.: pressure 150, clear fluid. Ratio 0.48 (0.48/0.48). 3rd ventricle 8 mm. No increase of surface air. Temperature 38.7°C . the day after. Otherwise no complaints.

Follow-up: admitted to a State mental institution at the age of $6\frac{1}{2}$ years. Developmental quotient 21. Since the age of 7 years paraplegia has been treated with splints. Understands something of what is said to him and plays a little. Has to be fed. Physical examination: head circumference 56 cm. Gait unsteady, usually on tiptoe. Feet in equino varus position. Very brisk patellar reflexes over an extended area. Bilateral ankle clonus and bilateral Babinski. Adduction of hips to about 100° . Reflexes in the arms normal. Eyes normal.

Diagnosis: spastic paraplegia, oligophrenia (idiocy).

Summary: a boy who was born by breech presentation 6 weeks prematurely and who had severe neonatal jaundice. Always mentally and physically retarded. *S.E.G.* at 5 years showed a ratio of 0.48, 3rd ventricle 8 mm. Is in a State mental institution. Has a developmental quotient of 21 and a spastic paraplegia.

142.

N.K. no. 08558/52. Girl born 19. 3. 51. No relevant familial predisposition. Only child. Pleurisy in the 5th month of pregnancy and pneumonia in the 5th-6th month. Delivery 6 weeks premature with asphyxia. Birth weight 1900 g.

Symptoms: had cyanotic episodes during the early days of life and was placed in an incubator. At the age of 7 months she had an episode in which her eyes flickered, she gave a jerk with her arms and became flaccid. Admitted to hospital and diagnosed as a case of petit mal. *E.E.G.* abnormal, chiefly in the left hemisphere. Eyes: atrophy of the optic nerves.

Admitted to N.K. department at the age of 10 months. Eye examination: atrophy of the optic nerves. Head circumference 44 cm. The skull was compressed from one side to the other. Hearing not reduced. There was bilateral Babinski and brisk tendon reflexes. X-ray of skull normal. *E.E.G.* not done.

S.E.G.: pressure 330. No entirely satisfactory A-P pictures but calculated on the two temporal horn pictures the ratio was 0.49 (0.49/0.48). 3rd ventricle 5 mm. No abnormal surface air. Temperature 38.3°C . the day after the examination, otherwise no complaints.

Follow-up: admitted to a State mental institution at the age of two years two months. Diagnosed as imbecility, blindness, internal hydrocephalus and spastic paraparesis. During admission she was not toilet-trained and was completely helpless. She could sit with strong support. Could see a little. Had had a single convulsion. Moved herself by crawling with the help of her arms. Could say single words. During the past year she has been in the cerebral palsy ward. Physical examination: happy and contented child. Gets along by crawling chiefly with help of her arms. Says hello and goodbye. Has a spastic tetraplegia which is most pronounced in the legs. No contractures. Head circumference 49 cm. No squint.

Diagnosis: oligophrenia (imbecility), tetraplegia (legs more affected than the arms), epilepsy.

Summary: a girl whose mother had a lung infection during pregnancy and whose birth was 6 weeks premature. Had cyanotic attacks during the first few days of life and seizures from the age of 7 months. *S.E.G.* at 9 months showed a ratio of 0.49, 3rd

ventricle 5 mm. She is in a State institution in a ward for cerebral palsied children. She is almost helpless.

143.

N.K. no. 03123/49. Girl born 6. 11. 45. No familial predisposition. Third of three children. Pregnancy and delivery normal. Birth weight 2850 g.

Symptoms: at the age of 7 months there were episodes during which the patient extended her arms over her head and the respiration became panting. Appeared convulsive in character. Brief loss of consciousness occurred on two occasions. Seizures occurred 4-5 times a day and started with a cry. She was very retarded mentally and physically and had to be fed. She could not turn herself over.

Admitted to N.K. department at the age of 3 years 3 months. Head circumference 50 cm. "Cracked pot" sound on cranial percussion. Eyes normal. Used the left-sided extremities more than the right. Doubtful right-sided Babinski, definite left-sided Babinski. X-ray of skull: large thin-walled with deep posterior fossa and coarse markings. E.E.G.: very severe diffuse dysrhythmia with low frequency and high amplitude.

S.E.G.: pressure 550, clear fluid. Ratio 0.50 (0.51/0.49). 3rd ventricle? Temperature 38.1° C. the same day, normal on the third day. Otherwise no complaints.

Follow-up: placed under State mental care at home. Died at home at the age of 5 years. Diagnosis: bronchopneumonia. Complication: generalised weakness. Cause of death: weakness due to pneumonia. No autopsy.

Diagnosis: cerebral palsy (? hemiplegia), oligophrenia (idiocy), epilepsy.

Summary: a girl who began to have convulsions at the age of 7 months. These increased over the years and she was very retarded mentally and physically. S.E.G. at the age of 3 years showed a ratio of 0.50. Died at home from pneumonia.

144.

N.K. no. 09826/52. Girl born 28. 1. 52. No familial predisposition. Second of three children. Pregnancy normal. Delivery one month premature, otherwise normal. Birth weight 2250 g.

Symptoms: slow weight gain. First focused at 4-5 months of age. Admitted to hospital and transferred to the R.H. Paediatric Department at the age of 8 months. E.E.G. showed severe focal dysrhythmia with spike focus over the left hemisphere. X-ray of skull showed a slightly flattened posterior fossa. While in hospital she had generalised spasmodic jerks. All the extremities were spastic.

Admitted to N.K. department at 9 months of age. Eye examination: atrophy of the optic nerve and convergent squint. Could not raise her head. Smiled and chattered. The hands were clenched and muscle tone was increased in the arms. In the legs there were adductor spasms and a tendency to right ankle clonus. Tendon reflexes brisk. No Babinski.

L.E.G.: pressure 170, clear fluid. Ratio 0.50 (0.50/0.50). 3rd ventricle 7 mm. No rise in temperature or other complaint.

Follow-up: Admitted to a State mental institution at the age of 20 months and died two months later. On admission head circumference was 42.5 cm. No eye signs. There was moderately increased muscle tone in all extremities. Understood what was said to her. Had occasional jerks in the arms and legs. During the last month her temperature rose but there were no signs of pneumonia. Thereafter the temperature dropped and was normal for a fortnight when it again rose to 39.5° C. and on this occasion there were signs of pneumonia. The patient's condition deteriorated and she died. No autopsy was performed.

Summary: a girl who was born a month prematurely and was always slow in development. Had seizures at the age of 8 months and spastic tetraplegia. L.E.G. at 9 months showed a ratio of 0.50, 3rd ventricle 7 mm. Placed in a State mental institution where she died at the age of 22 months after a febrile episode.

145.

N.K. no. 21738/54. Girl born 28. 7. 52. Familial predisposition: father's brother had convulsions. Pregnancy normal. Birth: transverse position and the child had to be turned and manually extracted, but there was presumably no asphyxia. Birth weight 3000 g.

Symptoms: convulsions occurred at the age of two days. Admitted to a neurosurgical department at the age of two months. Sub-dural puncture showed no abnormality. Admitted at a little more than a year to the R.H. Paediatric Department. Sub-dural puncture continued to be normal. X-ray of skull showed scaphocephaly. E.E.G. showed severe depression of activity particularly over the right hemisphere. L.E.G.: severe dilatation of the ventricular system. Ratio approximately 0.50. 3rd ventricle 10 mm.

Admitted to N.K. department at the age of 17 months. Eye examination: possible bilateral disc atrophy, possible blindness. Right half of the skull prominent. Circumference 45 cm. It was not possible to make any contact with the child. She did not react to light or sound. She had a spastic tetraplegia. No further examination was carried out as L.E.G. had been performed earlier. She was later admitted because of a possible increased distance between the arches of the cervical vertebrae but this was thought to be within normal limits for her age.

Follow-up: after admission to the R.H. Paediatric Department she was admitted to a State mental institution where she stayed until her death at the age of 3 years 10 months. Diagnosed as a case of oligophrenia (idiocy), quadriplegia. She had been very upset by the journey and was almost moribund on admission. She was described as a small and very sick, chronic mental case. She was bedridden and had periods of fever. Would hardly eat and gradually went downhill. Could not talk and did not understand what was said to her. No contact was possible. Spasmodic jerks occurred now and then. Diagnosis: emaciation, bronchopneumonia. No autopsy performed.

Diagnosis: spastic tetraplegia, oligophrenia (idiocy), epilepsy, microcephaly.

Summary: a girl with a paternal family history of convulsions. She was in the transverse position at birth. Convulsions occurred at the age of 2 months and she did not develop mentally and had a spastic tetraplegia. L.E.G. at the age of one year showed severe dilatation of the ventricular system, ratio 0.50, 3rd ventricle 10 mm. Placed in a State mental institution where she died when nearly 4 years old possibly due to bronchopneumonia.

146.

N.K. no. 08218/51. Girl born 18. 12. 50. No familial predisposition. Second of three children, twin A. (Twin B. was stillborn and severely macerated). Pregnancy: oedema but no albuminuria. Tonsillitis two days before delivery which was said to be 3 weeks premature. Birth weight 2600 g.

Symptoms: examined as an out-patient in the R.H. Paediatric Department at the age of 6 months when the mother thought that mental development was slow. The child was found to be severely oligophrenic and was admitted to the department at the age of 6 months. She could not sit up or grasp objects. X-ray of the skull and eye examination showed no abnormality. E.E.G.: the most severe degree of focal dysrhythmia.

Admitted to N.K. department at 10 months. Clonic jerks in the extremities seen during examination. Eyes: possible blindness. Did not appear to follow light. Head circumference 44 cm. Appeared oligophrenic. Reflexes normal.

S.E.G.: pressure 250, clear fluid. No really satisfactory pictures obtained. Dilatation was severe. Ratio 0.52 (0.53/0.51). 3rd ventricle 9 mm. Only slight surface air. No temperature or other complications following the examination.

Follow-up: admitted to a State mental institution at the age of a year. Eyesight found to be decreased on admission and examination the following year showed atrophy of the optic nerve. During the same year there were two petit mal episodes and at 2½ years she had a generalised convulsion. Her condition deteriorated, she was very difficult to feed and she lost weight. Physical examination: the patient was blind and there was nystagmus. She looked dull and in poor general condition, could not talk and did not understand anything. Did not co-operate with the examiner and became extremely

rigid when touched. Hip abduction about 20° . Early contractures of the ankle joints were present. Head circumference 48.6 cm. Reflexes very brisk.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, blindness and epilepsy.

Summary: a girl who was the first of twins, the second being stillborn. Pregnancy was complicated by oedema. When 6 months old she was found to be retarded. S.E.G. at 10 months showed a ratio of 0.52, 3rd ventricle 9 mm. There was a severe degree of spastic tetraplegia present. Placed in a State mental institution where she was found to be blind. Continued to have seizures and condition is deteriorating.

147.

N.K. no. 01347/48. Boy born 28. 7. 44. No familial predisposition. Second of three children. Pregnancy complicated by oedema, nausea and vomiting. Birth: the head was fixed and injections had to be given. Delivery lasted two hours but there was no asphyxia. Birth weight 4100 g.

Symptoms: walked at 8 months, talked and was toilet trained at a year. Had always had rather a large head but at the age of a year it appeared to be increasing too rapidly and he was therefore admitted to R.H. Paediatric Department where he was treated by radiotherapy. Was followed up at yearly intervals. Head circumference at 13 months was 55 cm., 20 months 58 cm., 3 years 2 months 61 cm., and 3 years 5 months 61 cm. X-ray of skull showed pronounced hydrocephalus. Eyes normal.

Admitted to N.K. department at the age of 3 years 8 months. Head circumference 62 cm. "Cracked pot" sound on cranial percussion on the right. Alert and lively but perhaps a little retarded. Gait unsteady and spastic. Tendon reflexes brisk and Babinski present on the left. Arms also spastic. E.E.G. not done. X-ray of skull showed it to be large and asymmetrical. Burr holes showed no sub-dural hygroma.

V.E.G.: pressure 160. Measurement not possible but there was enormous dilatation particularly of the left lateral ventricle and ratio here was 0.60, 3rd ventricle 20 mm. There was possibly a sub-dural air collection and a cyst on the right side.

Operation over the anterior part on the right side: entry was made into a large bluish cyst which lay basally and frontally. The cortex was thin and pushed upwards. The cyst contained fluid and continued into the right lateral ventricle and through the septum pellucidum into the left lateral ventricle. Microscopy showed it to be an arachnoid cyst. The temperature was raised to a maximum of 39.2°C . for 10 days after the operation but there were no other complications.

Follow-up: examined in the Orthopaedic Hospital's cerebral palsy clinic at the age of 8 years 10 months. Head circumference 63.5 cm. Slight spastic tetraplegia and debilitas mentis. Placed under mental care in a boarding school from the age of 10 years 10 months to 11 years 6 months and then in a special day school. I.Q. at 10 years 6 months was 53 and a year later 61. The family thought that progress had been made particularly after the child started at the day school. He is happy and contented and has no seizures. He had no real motor difficulties but finds finger movements hard. Physical examination: head circumference 63.5 cm. No eye signs. Tendon reflexes brisk in the arms, particularly on the right. The gait is somewhat broad-based and stiff with a slight tendency to walk on the toes on the right side. Runs fairly well and only falls occasionally. Patellar reflexes brisk particularly on the right where they can be elicited over the whole tibia. Ankle clonus present on the right side, doubtful on the left. Bilateral Babinski. Speech is good and understanding excellent. Appears more intelligent than I.Q. assessment would indicate.

Diagnosis: spastic tetraplegia (more pronounced on the right), oligophrenia (debilitas mentis).

Summary: a boy whose mother was sick during pregnancy and whose head was fixed during delivery. At the age of a year increasing head circumference was noted. V.E.G. at 3 years 8 months showed a ratio of 0.60, 3rd ventricle 20 mm. A right-sided arachnoid cyst was found communicating with the ventricular system. He has no seizures and only slight spastic tetraplegia. He is under State mental care and attends a special day school.

148.

N.K. no. 03327/49. Boy born 1.3.49. No known familial predisposition. Fourth of four children. Pregnancy normal but delivery 4 weeks premature and lasted 26 hours. Injections given. The cord was round the neck and the child was asphyxiated. Birth weight 2650 g.

Symptoms: 3 days after birth had convulsions with extension of right arm and flexion of left arm, nystagmus, neck stiffness and colour change. Repeated sub-dural puncture and lumbar puncture showed bloodstained yellow fluid. The condition became worse and he was admitted to the R.H. Paediatric Department.

Admitted to N.K. department at 2 weeks of age. Transitory convergent squint present. Head circumference 36 cm. Neck stiffness. No abnormality on neurological examination. Cisternal puncture showed bloodstained fluid. Many episodes of one-sided colour change.

V.E.G.: pressure not increased. Fluid yellow. Ratio 0.68 (0.69/0.67). 3rd ventricle 4 mm. No complications following the examination.

Follow-up: discharged to a paediatric department where he died during a cyanotic attack at two months of age after gradual deterioration. The temperature was usually sub-normal. Autopsy: sequelae of sub-arachnoid haemorrhage, occlusion of the foramen Magendie and Luscha, severe internal hydrocephalus, severe atrophy of the cerebral cortex. The autopsy reported nothing abnormal to be found other than in the brain. Ochre-coloured membranes were found below the right hemisphere, particularly over the pons and pedunculi. The cortex was 2-4 mm. thick. The cavities were filled with yellow serous fluid. Microscopy not performed.

Diagnosis: rigidity, epilepsy.

Summary: a boy whose birth was said to be 4 weeks premature. The cord was round the neck and he was asphyxiated. Convulsions occurred 3 days after birth and there was neck stiffness. V.E.G. at two weeks showed a ratio of 0.68, 3rd ventricle 4 mm. He was discharged to a paediatric department where he died at the age of two months during a cyanotic attack.

149.

N.K. no. 06604/50. Boy born 25.8.50. No familial predisposition. Third of three children. Pregnancy complicated by pain. Birth 4 weeks premature, medically induced, difficult and by breech presentation. Fairly severe asphyxia present. Birth weight 2500 g.

Symptoms: flaccid and cyanotic at birth and immediately admitted to paediatric department. There were many cyanotic attacks during the first weeks and the head circumference increased very rapidly. Spinal puncture and right sub-dural puncture showed cloudy, yellow fluid. There was no fluid on the left side. Head circumference 47.5 cm. when the patient was about 3 months old. Increased 1.5 cm. in one week.

Admitted to N.K. department at 3 months of age. Eye examination normal. Head circumference 47.5 cm. No bulging of the fontanelles. Slight neck stiffness. Bilateral Babinski. X-ray of skull and E.E.G. not done.

V.E.G.: pressure 120, clear fluid. Ratio 0.69 (0.70/0.67). 3rd ventricle 13 mm. Was in poor general condition after the examination and had neck stiffness for 8 days afterwards. Temperature was 38.5° C. the same day and remained raised for 8 days.

At that time coagulation of the choroid plexus on the left side was performed followed by right-sided craniotomy a fortnight later because of rapid increase in head circumference. The cortex was only 7 mm. thick. A purulent meningitis with innumerable cocci and leucocytes together with fibrin membranes was found. No further exploration undertaken. Post-operatively he was semi-comatose, febrile and very rigid and had a number of convulsions.

Follow-up: discharged to a paediatric department where he stayed until he died at the age of 11 months. He had numerous generalised convulsions, was rigid and often lay in opisthotonus position. Head circumference at 9 months was 49.5 cm. His condition gradually deteriorated and he died apyrexial. Autopsy: severe internal hydrocephalus and cerebral atrophy, moderate degree of localised purulent meningitis and partial atelectasis of the lungs. Examination of the brain revealed severe dilatation of the lateral ventricles

on both sides and pronounced cortical atrophy. On the right side posteriorly there was in addition thin pus. Microscopy not performed.

Diagnosis: rigidity, epilepsy.

Summary: a boy whose mother had pain throughout the entire pregnancy. Birth difficult with breech presentation and asphyxia. Immediately after birth had flaccidity and cyanosis. V.E.G. at age of 3 months performed because of increasing head circumference, ratio 0.69, 3rd ventricle 13 mm. Coagulation of the left choroid plexus and right-sided craniotomy performed. Remained in a paediatric department until his death at the age of 11 months.

150.

N.K. no. 23201/55. Boy born 6. 5. 53. Familial predisposition: father's sister a congenital mental defective. Fourth of four children. Pregnancy and birth normal. Birth weight 4250 g.

Symptoms: had bilateral acute otitis media at 7 months of age followed three days later by Pfeiffer meningitis and admission to hospital for two months. Examined in a neurosurgical department for hydrocephalus. L.E.G: severe symmetrical dilatation of the ventricular system. No air on the surface. Admitted to the R.H. Paediatric Department from the age of 18 months to nearly two years. E.E.G. severely abnormal. L.E.G: enormous dilatation. Ratio 0.64 (0.70/0.57).

Admitted to N.K. department when two years old. Head circumference 47 cm. Spastic tetraplegia more pronounced on the left than the right. Eyes normal. E.E.G. severely abnormal. X-ray of skull normal.

V.E.G: pressure 0, clear fluid. Ratio 0.71 (0.71/0.71). 3rd ventricle 12 mm. Temperature 40.2° C. the day after, normal on the third day. During the examination the dura was opened and an increased quantity of clear fluid was found. Cortical biopsy showed chronic meningitis.

Follow-up: discharged home from the R.H. Paediatric Department and from there admitted to a State mental institution at the age of 2½ years. Diagnosed as a case of oligophrenia (idiocy). He had a fracture of the right femur and was completely helpless. Investigated for Addison's disease because of brownish pigmentation but this was not proved. Physical examination: in poor condition. Eyes appeared very expressive. Screamed at the slightest touch. Pigmentation of hand and fingers present. Head circumference 44.6 cm. Very thin, particularly in the legs. Prognosis for life must be considered very poor.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, microcephaly.

Summary: a boy whose father's sister was mentally defective. At 7 months had Pfeiffer meningitis after which severe dilatation of the ventricular system was found. V.E.G. at the age of almost two years showed a ratio of 0.71, 3rd ventricle 12 mm. Cortical biopsy showed chronic meningitis. Is in a State mental institution, has a severe spastic tetraplegia and is completely helpless.

151.

N.K. no. 23419a/55. Boy born 31. 8. 52. Familial predisposition: cousin is a mongoloid idiot. Second of two children. Pregnancy and birth normal. Birth weight 3050 g.

Symptoms: at the age of two months it was noticed that the eyes were rotating and he was admitted to a paediatric department. A positive toxoplasmosis reaction was found in the mother. At the age of 22 months had grand mal seizures followed by minor seizures. Treated in the R.H. Paediatric Out-patient Department from the age of 2 years 3 months. Undulating nystagmus was present. Head circumference 50 cm. Muscle tone generally increased. Bilateral ankle clonus. Diagnosed as a case of spastic tetraplegia. Admitted to the R.H. Paediatric Department at the age of 2 years 8 months. E.E.G. severely abnormal, diffuse with a spike focus in the left temporal region. X-ray of skull showed no calcification. *Diagnosis:* congenital toxoplasmosis and bilateral chorioretinitis.

Admitted to N.K. department at the age of 2 years 9 months.

V.E.G: on puncture the cortex was found to be thin and on biopsy entry was made

into the ventricle. Clear fluid was present. The system was enormously dilated with only a 5 mm. cortical brim. Ratio 0.80 (0.80/0.80). 3rd ventricle 26 mm. Temperature 39.3°C . the day after and fever continued for several days.

Second admission to N.K. department at the age of 2 years 10 months to decide whether the condition was due to a stenosis of the aqueduct. Puncture made through the V.E.G. holes: pressure on the left side 300, right side 150. Lumbar puncture: pressure 300. Positive Queckenstedt. Air could be injected into the ventricles so a stenosis was therefore excluded. Biopsy from the left occipital region showed chronic meningo-encephalitis. It was not possible to decide whether this was a case of toxoplasmosis. No fever or other complications following the examination.

Follow-up: admitted to the R.H. Paediatric Department at the age of 4 years for about 6 months. Eye examination: coloboma-resembling atrophy; no new changes. E.E.G. still severely abnormal. X-ray of skull unchanged. Convulsions controlled by phenobarbitone. Head circumference 53 cm. Nystagmus present. Almost no spontaneous movement. Recommended for State mental care. After discharge the mother thought that the condition was fairly static, in any case to start with. There were almost no convulsions but there was no mental development.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, epilepsy, eye changes (? sequelae of chorio-retinitis), ? toxoplasmosis. The reason for the uncertainty of the last diagnosis is that at this point it has not been possible to prove a positive serum reaction in the child but only in the mother. The diagnosis was based alone on the eye examination.

Summary: a boy whose cousin is a mongoloid idiot. Rotatory movements of the eyes noticed at the age of two months. When almost two years old had grand mal seizures and was diagnosed as a case of spastic tetraplegia. V.E.G. when nearly 3 years old showed a ratio of 0.80, 3rd ventricle 26 mm. Microscopy showed chronic meningo-encephalitis. Is under State mental care at home. Has no seizures but has made no progress.

152.

N.K. no. 07392/51. Boy born 9.2.51. No familial predisposition. Only child. Pregnancy normal. Birth difficult, lasted 50 hours. No asphyxia. Pressure marks present on the head. Birth weight 3575 g.

Symptoms: tendency to opisthotonus since birth. At the age of 9 days convulsions occurred and he was admitted to hospital. There were repeated generalised convulsions. Lumbar puncture when the child was 13 days old showed an increased number of polynuclear cells. No bacterial growth. Thought to be a case of meningitis and treated by antibiotics. Admitted to R.H. Paediatric Department at the age of two months. Still constant opisthotonus and increasing dullness and rigidity.

Admitted to N.K. department at 3 months of age. Head circumference 44 cm. Lay in opisthotonus position. Eye examination normal. Muscle tone generally increased. Reflexes could not be assessed. E.E.G. not done.

V.E.G.: pressure 420, clear fluid. The pictures showed an enormous dilatation of the whole system. Ratio about 0.95 (0.95/0.95). No complications after the examination.

Follow-up: admitted to a State mental institution at the age of 18 months and died the day after admission. Physical examination: head circumference 89 cm. All extremities spastic. Reflexes could not be elicited. In both parietal regions there was an area of gangrenous ulceration, a hand's breadth in size. Temperature rose to 38.4°C . and he died. No autopsy was performed.

Diagnosis: spastic tetraplegia, oligophrenia (? idiocy), epilepsy.

Summary: a boy whose delivery was difficult and long-lasting and who had convulsions and opisthotonus from birth. Possible meningitis at two weeks. V.E.G. at 3 months showed almost total dilatation of the system. Ratio 0.95. Admitted to a State mental institution and died at the age of 18 months the day after admission.

153.

N.K. no. 8629c/46. Girl born 29.12.21. No familial predisposition. No information on pregnancy. Delivery normal. Birth weight unknown.

Symptoms: during the second year of life fell downstairs and hit her head. 30 minutes

after the fall she vomited, lost consciousness and had jerks down the right side. The episode lasted 3 hours. She was then symptom-free until the age of 9 years when episodes of petit mal occurred, increasing to a couple of times a week. In addition there were brief convulsions involving the right hand once or twice a week without any loss of consciousness. After another fall she was blind for 15 minutes. From the age of 12 years she had right-sided convulsions with loss of consciousness lasting from 1-3 minutes. Intellectually normal and did well at school. Admitted to a neurological department at the age of 11, 12 and almost 15 years and then to the R.H. Neuromedical Department.

Admitted to N.K. department when almost 15 years old. There was a scar over the vertex. Eyes normal. Reflexes: brisk tendon reflexes, otherwise normal. X-ray of skull normal.

V.E.G.: ratio 0.30 (0.29/0.31). 3rd ventricle 3 mm. Left side - 10 mm. No complications after the examination.

Second admission to N.K. department four months later for arteriography. She had had two seizures shortly after discharge. Bilateral arteriography showed that the condition was probably one of an atrophic lesion anteriorly in the left hemisphere.

Operation over the anterior part of the left hemisphere. Clear signs of an old fracture were found and corresponding to this there was a fibrous connection between the scar and the cortex. There were two large veins in the adjacent area and in addition a collection of fluid. A pea-sized typical fibrous traumatic lesion was found and removed.

Third admission to N.K. department at the age of 23 years. The patient had been treated for pains in the joints of the hand at the age of 20 years. The attacks of petit mal were becoming more rare and there had been no real convulsions for about a year. There had, however, been increasing headache and blackness before the eyes. Physical examination: eye examination normal. X-ray showed sequelae of craniotomy. E.E.G. showed diffuse dysrhythmia.

S.E.G.: pressure 120, clear fluid. Ratio 0.31 (0.28/0.34). 3rd ventricle 5 mm. Left side - 15 mm. Temperature 38.1° C. after examination.

Fourth admission to N.K. department at 25 years. Admitted because of seizures and headache for nine months. Eye examination and reflexes normal. E.E.G. showed severe dysrhythmia. No further investigation undertaken.

Follow-up: patient was investigated in a medical out-patient department at the age of 29 and 33. The next year she was found unconscious and brought into a casualty department where she was found to be dead. Autopsy: the scar of previous arteriography could be seen on the neck. Both carotid arteries were narrowed and obliterated. The cranium was opened and the meninges found to be normal. The brain itself showed some oedema and hyperaemia with cone formation. On the surface on the left side between the frontal and temporal lobe was an area resembling a scar. In addition there were scattered small haemorrhages. The brain vessels showed no definite abnormality and microscopy of the pituitary was normal. The rest of the autopsy revealed hyperplasia of the liver, bronchitis and gallstones.

Diagnosis: epilepsy, headache.

Summary: a girl who during her second year of life sustained a head injury with subsequent vomiting, loss of consciousness and convulsions. From the age of 9 years she had increasing convulsions of the petit mal and Jacksonian type. V.E.G. at 15 years showed a ratio of 0.30, 3rd ventricle 3 mm. Left side - 10 mm. Operation the following year showed a fibrous, traumatic lesion frontally on the left side. Over the following year she continued to have seizures and headaches. At the age of 33 she was dead when brought to a casualty department.

154.

N.K. no. 21091/53. Boy born 6. 3. 53. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3250 g.

Symptoms: sustained a head injury at the age of two months. When almost three months old had fever and possible left-sided pneumonia. Admitted to hospital where he had neck and back stiffness and grimacing. Lumbar puncture showed yellow fluid, 700/3 cells. Treated with antibiotics. Transitory small jerks in both arms and down the right

side of the face were noticed. Transferred to the R.H. Paediatric Department. E.E.G. showed severe focal dysrhythmia. Skull X-ray normal. Eyes: paresis of movements to the right. Sub-dural puncture showed yellow fluid.

Admitted to N.K. department at 5 months. Head circumference 42 cm. Eyes normal. Normal movements of all extremities. Sub-dural puncture showed clear fluid.

V.E.G.: pressure 100, clear fluid. Ratio 0.30 (0.29/0.32). 3rd ventricle 8 mm. Left side - 5 mm. On the right side there was a large, triangular air collection over the Sylvian fissure. No fever or other complications after the examination.

Right-sided arteriography showed displacement corresponding to the atrophic lesion.

Follow-up: developed well both physically and mentally, and understands all that goes on round him. Walked at 15 months and said single words at 3 years though no real sentences. No seizures or headaches. Enjoys other children's company and is very independent. Is toilet-trained and can almost dress himself. Prefers to use his left hand. Physical examination: appears healthy. Head circumference 48.8 cm. Eyes normal. Reflexes: ankle clonus on the right, no Babinski. All other reflexes normal. Uses both hands well and walks well. It is rather difficult to assess his mental capacity because of the speech retardation. Would seem to be a little retarded.

Diagnosis: dysarthria (speech retardation), slight right-sided hemiplegia, possible intellectual inferiority.

Summary: a boy who at two months of age sustained a head injury and at three months had an infection with a possible meningeal reaction followed by small jerks. *V.E.G.* at 5 months showed a ratio of 0.30, 3rd ventricle 8 mm. Left side - 5 mm. There was localised air over the Sylvian fissure. Has since developed well. Speech and mental development somewhat retarded.

155.

N.K. no. 22139/54. Girl born 9. 11. 40. No familial predisposition. Third of five children. Pregnancy complicated by erythema nodosum and albuminuria. Birth difficult, breech presentation and intra-cranial haemorrhage said to have occurred. Birth weight 2900 g.

Symptoms: there was severe jaundice and she was immediately admitted to the R.H. Paediatric Department. Hemianopia found during infancy. Always used her right hand. At the age of 7 years was in a children's convalescent home because of nervousness after otherwise normal development. About 13 years old attacks resembling petit mal began to occur many times a day. Admitted to a medical department where E.E.G. revealed a left-sided temporal focus and eye examination a homonymous right-sided loss of vision.

Admitted to N.K. department when nearly 14 years old. Normal appearance but perhaps a little retarded. Eye examination: right-sided homonymous hemianopia, convergent squint, left-sided amblyopia and nystagmus on looking to the left. Left-handed. Slight right-sided dysidiadokokinesis. Doubtful Romberg. No Babinski. Head circumference 50 cm. X-ray of skull normal. E.E.G.: on the left side there was almost total depression of alpha activity. Left-sided arteriography was normal.

V.E.G.: pressure 250, clear fluid. Ratio 0.30 (0.29/0.32). Left side - 15 mm. 3rd ventricle 8 mm. Pronounced dilatation posteriorly on the left side. Temperature 38.1° C. the same day, normal thereafter and no other complications.

Follow-up: has done well since. Left school at 13 because of seizures. Began training as a children's nurse at the age of 15 years. E.E.G. repeated on many occasions last showed a moderate degree of abnormality with a low frequency focus in the left temporal region. Is taking phenobarbitone. Has been in a special school and will be returning to nursing. Seizures are very infrequent and usually occur pre-menstrually. Does well without glasses and the hemianopia does not trouble her. She is left-handed but frequently uses her right hand. Physical examination: physical development completely normal. Head circumference 52 cm. Somewhat brisk right-sided tendon reflexes but no hemiplegia.

Diagnosis: epilepsy, slight right-sided neurological changes.

Summary: a girl whose mother had albuminuria and erythema nodosum during pregnancy. Delivery was by breech presentation and difficult and there was severe jaundice. From the age of 13 years seizures resembling petit mal occurred daily. *V.E.G.* at that time

showed a ratio of 0.30, 3rd ventricle 8 mm, left side - 15 mm. At follow-up she had done well. She had begun training as a children's nurse and had only rare seizures. Physical examination showed only slight right-sided reflex changes.

156.

N.K. no. 1181/38. Girl born 7. 6. 32. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: from early childhood had generalised tonic and clonic convulsions in connection with fever. Admitted to a paediatric department at the age of 3 years 2 months and to an infectious diseases hospital and neurological department three years later. Convulsions accompanied by loss of consciousness and incontinence of urine and faeces. They sometimes occurred at intervals of several days but could occur every hour. While in hospital numerous attacks of petit mal were observed. In addition there were many minor seizures with tonic spasms, mostly on the left side. Could be very undisciplined, noisy and destructive.

Admitted to N.K. department at the age of 6 years. Appeared very retarded and made a number of scenes. Eye examination normal. Neurological examination normal. X-ray of skull normal.

V.E.G.: normal pressure. Ratio 0.31 (0.32/0.31). 3rd ventricle 4 mm. Left side - 11 mm. Rather pronounced surface air, mostly on the left side. Temperature 38.8° C. the same day, normal two days later, and no other complications.

Follow-up: attended an ordinary school until the age of 8 years, after which she went into a special class. I.Q. at 7 years was 84 and a year later 73. Did well in the special class and was described as a lively, somewhat aggressive and nervous child. Had the will to do things but worked poorly. Physical development and general health are good. No convulsions at school and presumably had the last when she was 6 years old. Has had various factory jobs since leaving school and is now married. Has no physical defects. Speech is normal. Occasionally complains of tired eyes. The patient has two children. The first, a 5-year-old girl, had a difficult delivery and developed convulsions at 6 days. She has been in an epileptic hospital for two years. The second, a boy, is 2½ years old and on examination appears to be healthy. Physical examination: head circumference 54 cm. Eyes and neurological examination normal. Appears of borderline intelligence.

Diagnosis: previous epilepsy, intellectual inferiority.

Summary: a girl who since early infancy had generalised febrile convulsions later developing into petit mal seizures and non-febrile convulsions. V.E.G. at 6 years showed a ratio 0.31, 3rd ventricle 4 mm., left side - 11 mm. No convulsions since the age of 6 years. She was put into a special class at the age of 8 years and did fairly well. She is married and has two children, one of whom has convulsions.

157.

N.K. no. 02207/48. Boy born 24. 2. 48. No familial predisposition. Only child. Pregnancy normal. Delivery full-term, difficult and lasted 54 hours. No asphyxia. Birth weight 4000 g.

Symptoms: jerking of all extremities since birth, occurring in series 5-10 times a day and accompanied by loss of consciousness. Severe mental retardation was noticed at 4-5 months and the neck muscles seemed particularly rigid. Admitted to the R.H. Paediatric Department at the age of 5 months. X-ray of skull and eye examination normal. Developmental quotient 28. Sub-dural puncture showed presumably normal conditions.

Admitted to N.K. department at 5 months. Eye examination normal. Lay in the opisthotonus position and had slight neck stiffness. Appeared dull.

V.E.G.: pressure 0, clear fluid. Ratio 0.31 (0.32/0.30). 3rd ventricle not measurable. Right side - 7 mm. No complications or rise in temperature after the examination. Burr hole performed in the right motor region. Cortex appeared normal.

Follow-up: stayed in a ward for chronic sick children and then transferred to a State mental institution for 16 months from the age of 17 months. Diagnosed as a case of imbecility. The patient then went with his family to Sweden and information has been obtained from there that he is still alive but it is not known whether he is under mental

care or not. This is almost certain to be the case, however, after earlier descriptions of his condition.

Diagnosis: oligophrenia (imbecility).

Summary: a boy whose delivery was difficult and prolonged. Convulsions occurred from birth and he was severely mentally retarded. V.E.G. at 5 months showed a ratio of 0.31, right side - 7 mm. Placed in a State mental institution at the age of 17 months but then moved with his family to Sweden where he still lives.

158.

N.K. no. 06872/51. Boy born 17.11.45. Familial predisposition: an older brother was operated on for cranial dysynostosis. Fourth of four children. Pregnancy normal. Birth 4 weeks premature, breech presentation. No asphyxia. Birth weight 3500 g.

Symptoms: shortly after birth he seemed dull and difficult to rouse. Development was slow. He walked at 22 months and talked at 3 years. At the age of one month had generalised convulsions. Admitted to hospital on several occasions because of them. Admitted to the R.H. Paediatric Department at the age of 5 years. E.E.G. showed severe dysrhythmia with a focus in the left frontal region. L.E.G. ratio 0.31 (0.30/0.32). 3rd ventricle not measurable. Left side - 8 mm. No abnormal cortical air.

Admitted to N.K. department at the age of 5 years 3 months. Used left hand more than right. Mentally normal though perhaps a little shy. Eye examination and skull X-ray normal. No definite reflex changes. Right side of mouth somewhat drooping. E.E.G. showed severe dysrhythmia. It was thought that there was a meningo-cerebral scar in the left pre-motor region. No further examinations performed.

Follow-up: no seizures from the age of 6 to 11 years. Then had a prolonged seizure localised to the right side and this was followed by several more at months' intervals. Anti-epileptic treatment resumed. Does fairly well at school but has some difficulty with reading and arithmetic. Physical examination: healthy, normal appearance. Right-sided ankle clonus. Right-sided Babinski. Patellar reflexes elicited over the whole tibia on the right side. Tendon reflexes in the right arm also very brisk. Normal on the left. Can walk, run and jump completely normally. Is left-handed. Has no balancing difficulties. Eye examination normal. No cranial nerve paresis. Head circumference 52.3 cm.

Diagnosis: epilepsy, neurological changes as found in right-sided spastic hemiplegia but no disturbance of function.

Summary: a boy delivered by breech presentation who was rather difficult to rouse almost from birth. Convulsions began at a month and motor development was slow. L.E.G. at 5 years showed a ratio of 0.31, left side - 8 mm. Seizures ceased at 6 years but reappeared at 11 years and anti-epileptic treatment was resumed. He does fairly well at school.

159.

N.K. no. 25141 c/56. Girl born 20.11.53. No familial predisposition. Only child. Pregnancy normal. Birth 4 weeks premature. No asphyxia. Birth weight 2930 g.

Symptoms: episodes of flaccidity and slight cyanosis from the age of 14 days accompanied by staring vision. No real convulsions. Lasted 2-3 minutes and occurred 5-6 times a day. Admitted at the age of two months to the R.H. Paediatric Department. Only one convulsion occurred when the respiration became snoring, there was possible loss of consciousness and muscle spasms were seen around the left eye. This lasted two minutes. Sub-dural puncture and X-ray of skull normal. E.E.G. showed severe left-sided dysrhythmia. Re-admitted to the R.H. Paediatric Department at 9 months because of increasing convulsions. E.E.G. showed slight right-sided preponderance with diffuse abnormal activity.

Admitted to N.K. department at the age of 10 months. Eye examination showed divergent squint. "Cracked pot" sound on cranial percussion. Head circumference 49 cm. X-ray of skull normal. Bilateral Babinski.

V.E.G. pressure 300, clear fluid. Ratio 0.31 (0.32/0.30). Right side - 6 mm. 3rd ventricle 12 mm. Increased surface air. Temperature 38.8° C. the day after, otherwise no

complications. A large porencephaly was seen in the left hemisphere communicating with the sub-arachnoid space.

Re-admitted twice within three weeks when 12 months old. Investigations as before.

Operation at 13 months of age. Left-sided temporal lobectomy. Large fluid collections over the whole cortex. Frontally there was yellow fluid sub-durally under a thin membrane. Hygroma emptied. In the left temporal lobe there were many scar-like areas. The temporal lobe was removed as much as possible frontally and backwards to the large veins. No post-operative complications. Temperature 38.1° C. for two days. Microscopy showed slight sub-pial glia proliferation.

Follow-up: examined in the R.H. Paediatric Department as an out-patient. At 18 months can sit alone and raise herself up. Says single words. Has no seizures. Has lately become very restless and aggressive. Was admitted four times to the N.K. Department at the age of 3 years and is now in a State mental institution. Diagnosed as a case of porencephaly. No treatment given. Physical examination: appears very retarded and says only single words. Can sit, stand and walk. Head circumference 54 cm. There is a possible right-sided homonymous hemianopia. Neurological examination otherwise normal.

Diagnosis: oligophrenia (idiocy), previous epilepsy.

Summary: a girl who from the age of 14 days had episodes of flaccidity and cyanosis. Convulsions became more epileptiform and increased in number. V.E.G. at 10 months showed a ratio of 0.31, right side—6 mm, 3rd ventricle 12 mm. A large porencephaly was found in the left hemisphere. Left-sided temporal lobectomy performed at 13 months. Continues to be severely retarded and is in a State mental institution.

160.

N.K. no. 22042 a/54. Boy born 17. 12. 47. No known familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 4400 g.

Symptoms: after prolonged whooping-cough at the age of a year the patient developed sudden high fever after a violent attack of coughing. He lost consciousness and was admitted to the R.H. Paediatric Department. A convulsion which began in the ambulance lasted five hours and was followed by paralysis of the right arm.

L.E.G.: ratio 0.31 (0.29/0.33). 3rd ventricle 5 mm. Left side—10 mm. During admission seizures resembling petit mal and lasting about a minute occurred 3–5 times a day and were accompanied by jerks in the right arm.

Admitted to the N.K. department at the age of 2½ years. Eye examination normal. Power slightly reduced in the right arm and leg. Left-sided Babinski and brisk tendon reflexes on both sides. Walked alone but unsteadily. E.E.G.: waking curve showed no definite abnormality.

S.E.G.: pressure 230, clear fluid. Ratio 0.32 (0.30/0.34). 3rd ventricle 6 mm. Left side—11 mm. No fever or other complications following the examination.

Left-sided arteriography showed that the first part of the anterior cerebral artery was displaced corresponding to the area of atrophy.

Second admission to the N.K. department at the age of 6 years 5 months. The seizures had increased in frequency and occurred almost daily, usually on the right side. He could not get on with other children and complained of various pains in the limbs. Eye examination normal. Head circumference 52 cm. Speech was slightly retarded. Slight uncertainty of right-sided finger-nose test. X-ray of skull normal. E.E.G. severely abnormal.

S.E.G.: pressure 250, clear fluid. Ratio 0.32 (0.30/0.33). 3rd ventricle 7 mm. Left side—6 mm. Temperature 38° C. the day after but no other complications.

Left-sided arteriography unchanged.

Follow-up: the patient was followed up in the N.K. Out-patient Department. E.E.G. at 8 and 8½ years was severely abnormal with spikes and low frequency, particularly in the left temporal region. He is on anti-epileptic treatment, has started school and is doing well.

Diagnosis: epilepsy, slight neurological changes on the right side but no real spastic hemiplegia.

Summary: a boy who at 15 months of age, after a long episode of possible whooping-cough, developed sudden fever and convulsions lasting five hours. L.E.G. at that

time showed a ratio of 0.31. S.E.G. at 2½ years showed a ratio of 0.32, 3rd ventricle 6 mm., left side - 11 mm. S.E.G. repeated four years later because of an increasing number of convulsions showed unchanged conditions. He is doing well on anti-epileptic treatment, has some neurological changes but no real spastic hemiplegia.

161.

N.K. no. 1951/40. Boy born 15. 11. 26. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: at the age of 18 months sustained a fractured skull on the left side followed by right-sided hemiplegia. Craniotomy performed with improvement in the paralysis. Concussion and amnesia at the age of 10 at which time he was kept in bed for a week. Two years before admission again sustained concussion and a fractured arm. After the skull fracture there had been a moderate right-sided hemiplegia and hemihypoplasia. Six years before admission there had been a definite petit mal attack followed during the next few years by episodes of headache. During the year immediately prior to admission the seizures had increased in frequency; there had been brief unconsciousness and generalised convulsions. Admitted to the R.H. Neurological Department at the age of 13 years 4 months.

Admitted to N.K. department at 13 years 6 months. Eye examination: right-sided homonymous hemianopia. Scar from craniotomy. Right-sided hemiparesis with atrophy and shortening, chiefly in the arm. Feet in equinus position and right-sided Babinski. X-ray of skull: prominence corresponding to the operation site with thinning over the defect and small areas of calcification at the base.

V.E.G.: ratio 0.32 (0.31/0.32). 3rd ventricle 4 mm. Left side - 15 mm. Particular dilatation of the left lateral ventricle superiorly. Temperature 38.8° C. the same day, normal the day after. Dura and arachnoid on the left side markedly thickened but less so on the right side.

Follow-up: did not do well at school and had difficulty in keeping up. Was in prison for five months because of car stealing. Admitted to the hospital for epileptics at the age of 21 and again at 22. Diagnosed as a case of traumatic epilepsy and epileptic deviation of the mental state. On examination he appeared to be psychopathic. He had a bilateral homonymous hemianopia and right-sided spastic hemiplegia. L.E.G. unsuccessful. E.E.G. doubtful dysrhythmia, no paroxysm. Continues on anti-epileptic treatment and obtains an invalid pension. Still has occasional seizures of a few seconds' duration without loss of consciousness. These can be provoked by nervousness, for instance on receiving the letter from the examiner. The seizures begin on the right side and become generalised. Has had no headache since last insufflation. Works as an errand boy. Physical examination: head circumference 59 cm. Right-sided hemiplegia most pronounced in the arm. Appears rather clinging but not retarded. Eye examination: right homonymous hemianopia.

Diagnosis: right spastic hemiplegia (arm more affected than leg), epilepsy, right homonymous hemianopia.

Summary: a boy who sustained a fractured skull at the age of 18 months with a consequent right-sided spastic hemiplegia. Petit mal began at the age of 7 years and increased over the next few years. Concussion at the age of 10 and again at about 11. V.E.G. ratio at 13½ years 0.32, 3rd ventricle 4 mm., left side - 15 mm. Continues to have minor seizures. Has an invalid pension and works as an errand boy. Still has signs of a right-sided spastic hemiplegia and hemianopia.

162.

N.K. no. 3059/42. Girl born 7. 2. 34. No familial predisposition. Pregnancy complicated by rubella, probably halfway through. Delivery: slight asphyxia and cord round the neck. Birth weight 2900 g.

Symptoms: head injury without loss of consciousness at the age of 4½ years. Six months later rapid growth was noticed with early onset of puberty, enlargement of breasts, and appearance of pubic hair. Over the next year she became restless and difficult to manage and had increasing difficulty in writing on the line.

Admitted to N.K. department at the age of 8 years. Uncooperative on physical examination. Neurological examination normal. Skull: slightly oxycephalic and asymmetrical. X-ray of skull: thin-walled with deep posterior fossa.

V.E.G.: pressure 190. Ratio 0.32 (0.33/0.31). 3rd ventricle 6 mm. Right side - 6 mm. Temperature 38.6° C. the day after, normal on the fourth day.

Follow-up: is under State mental care at home. Menstruated at 8 years. Investigated by a gynaecologist but no abnormality found apart from precocious puberty. In particular there was no sign of an intra-cranial tumour. She is good at home and enjoys helping. Is rather slow at understanding and says very little herself but what she says is clear and sensible. Physical examination: big, strong girl. Height over 180 cm. Head circumference 55 cm. Reflexes brisk but not pathological. She was slow to answer a question and used only few words in reply.

Diagnosis: intellectual inferiority (? debilitas mentis), precocious puberty.

Summary: a girl whose mother had rubella halfway through pregnancy and who was slightly asphyxiated at birth. Six months after a head injury at the age of 4½ years she grew rapidly and developed precocious puberty. *V.E.G.* at 8 years showed a ratio of 0.32, 3rd ventricle 6 mm., right side - 6 mm. She is under State mental care at home, is rather slow to react and does not say very much.

163.

N.K. no. 02455/48. Boy born 22. 7. 48. No known familial predisposition. Fourth of four children. Mother had pyelitis during pregnancy. Delivery normal. Birth weight 3770 g.

Symptoms: 3 days after birth he had tonic jerks in all extremities. No jaundice. Admitted to hospital and during the next 3-4 weeks the convulsions became clonic and generalised. Transferred to the R.H. Paediatric Department at the age of about a month. Lumbar puncture normal. Subdural puncture: clear fluid on the right side, none on the left. X-ray of skull and eye examination normal.

Admitted to N.K. department at two months of age. Small, emaciated child with somewhat retarded physical development. Sub-dural puncture: clear fluid.

S.E.G.: ratio 0.33 (0.32/0.36). 3rd ventricle not measurable. Left side - 6 mm. No temperature or other complications.

Follow-up: discharged to another hospital where he died after only a few days at the age of three months. During his stay he had been very ill with grimacing, restlessness and generalised clonic convulsions. Temperature rose to over 40° C. and cyanosis occurred. No autopsy.

Diagnosis: encephalopathy, epilepsy.

Summary: a boy whose mother had pyelitis during pregnancy. Convulsions occurred from the third day of life and increased in number. *S.E.G.* at two months showed a ratio of 0.33, 3rd ventricle not measurable, left side - 6 mm. He died in hospital at the age of three months in hyperpyrexia with continuous convulsions and cyanosis.

164.

N.K. no. 05768/50. Girl born 10. 7. 48. No relevant familial predisposition. Fifth of five children. Pregnancy and birth normal. Birth weight 3500 g.

Symptoms: was quite well apart from otitis media at the age of five months. Always somewhat retarded, however, and from the age of one year had seizures resembling petit mal during which the head fell forward, there was colour change and the patient became withdrawn.

Admitted to N.K. department at the age of two years. Appeared an imbecile. Could only focus for a moment and did not grasp objects. Could walk with support. Eye examination: hypermetropia, decreased vision. X-ray of skull: increased digital markings. *E.E.G.*: pronounced side difference with low frequency over most of the right hemisphere.

V.E.G.: pressure 100. Ratio 0.33 (0.35/0.31). 3rd ventricle 3 mm. Right lateral ventricle angles more rounded and dilated than the left. Right side - 8 mm. No complications.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Under State mental care at home since the age of three years. Still has daily seizures with

stiffening down the left side and jerks on the right. Motor ability is satisfactory. She understands most of what is said and is very obedient. Mental development at the age of 9 years corresponds only to that of a 3-year-old. Physical examination: left spastic hemiplegia. Eye examination: eye movements normal.

Diagnosis: oligophrenia (imbecility), epilepsy, left spastic hemiplegia.

Summary: a girl who since the age of a year had seizures resembling petit mal and who was said to have always been retarded. V.E.G. at two years showed a ratio of 0.33, 3rd ventricle 3 mm., right side—8 mm. She is under State mental care at home. Continues to have seizures, has a left-sided spastic hemiplegia and is mentally retarded.

165.

N.K. no. 07657/51. Boy born 26. 12. 50. No familial predisposition. Third of three children. Pregnancy: toxæmia and skin irritation the whole time. Delivery very quick, otherwise normal. Birth weight 3200 g.

Symptoms: was remarkably quiet. At about the age of 11 days there was bleeding from the umbilical cord and he was therefore admitted to hospital and given a blood transfusion. At the same time there was severe jaundice and the child was almost green in colour which was thought to be caused by a partial atresia of the bile duct. At the age of 4 months rapid increase of head circumference was noticed. Motor development was retarded. He could lift his head up but could not sit. Recognised mother, focused and grasped objects.

Admitted to N.K. department at the age of 7 months. Eye examination showed no definite abnormality. Head circumference 44 cm. Right parieto-occipital region flattened. Happy, smiling child who made attempts to sit up. Movements equal on both sides. Reflexes: no definite abnormality.

V.E.G.: pressure 100, bloodstained fluid which quickly cleared. Ratio 0.33 (0.34/0.31). 3rd ventricle 9 mm. Right side—5 mm. No cortical atrophy. Temperature 38.5° C. the same day, 38° C. the next day. No other complications.

Follow-up: walked at the age of a year. Has developed completely normally and has no seizures. Can be rather bad-tempered. Is about to start school. Physical examination: head circumference 51 cm. Eye and neurological examination normal.

Diagnosis: healthy.

Summary: a boy whose mother had toxæmia during the entire pregnancy. Haemorrhage from the umbilical cord occurred at 11 days together with increasing jaundice. The head grew very fast at 4 months and V.E.G. was performed. Ratio was 0.33, 3rd ventricle 9 mm. and right side—5 mm. Later development was entirely normal and examination showed no abnormality.

166.

N.K. no. 22498/54. Boy born 29. 3. 53. No familial predisposition. Fourth of four children. Pregnancy normal. Delivery: face presentation. No complications. Birth weight 3350 g. Was blue at birth but cried immediately.

Symptoms: delayed development noticed when he was 9 months old. Sat alone at 12 months but could not walk or stand at 18 months. Said to recognise his parents. Admitted to the R.H. Paediatric Department at the age of 17 months because of episodes resembling petit mal occurring several times a day. E.E.G. showed no definite abnormality. X-ray of skull normal. L.E.G.: no ventricular filling, increased surface air.

Admitted to N.K. department at the age of 18 months. Eye examination: left divergent squint. Head circumference 50 cm. Appeared somewhat oligophrenic and cried a great deal. Could sit alone. Would not play. Bilateral Babinski. E.E.G. normal. Sub-dural puncture: clear fluid.

S.E.G.: air only on the convexity.

V.E.G.: pressure 250. Ratio 0.33 (0.32/0.33). Right side—5 mm. 3rd ventricle 8 mm. After S.E.G. temperature was 39.3° C., normal on the second day and no other complications. After V.E.G. the temperature was 38.1° C. the same day, otherwise no complications.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Continues

to have convulsions in spite of treatment with phenytoin. Is not spastic but very retarded. Sight and hearing normal.

Diagnosis: oligophrenia (? imbecility), epilepsy.

Summary: a boy delivered by face presentation. Retarded development noticed when he was 9 months old. Petit mal began at the age of about a year. V.E.G. at 18 months showed a ratio of 0.33, right side - 5 mm., 3rd ventricle 8 mm. Continues to have convulsions and is very retarded.

167.

N.K. no. 23101/55. Boy born 12.7.54. No known familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3400 g.

Symptoms: fell in his playpen at the age of 5 months and probably hit his head. During the six weeks before admission had almost daily seizures with jerks in the arms lasting 5-6 minutes. The seizures began with a few seconds' crying, he became withdrawn and probably unconscious. No post-paroxysmal complaints. Admitted to the R.H. Paediatric Department at the age of 7 months. E.E.G. severely abnormal. Eye examination and X-ray of skull normal.

Admitted to N.K. department at 8 months. Eyes normal. Head circumference 47 cm. All movements and reflexes normal. E.E.G. severely abnormal.

V.E.G: pressure 200, clear fluid. Ratio 0.33 (0.31/0.35). 3rd ventricle 4 mm. Left side - 5 mm. Temperature 39.4° C. the day after, normal on the fifth day. Otherwise no complications. Microscopy from cortex showed normal conditions.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. No seizures since discharge. On physical examination he appears completely normal. Walked alone at the age of 15 months. E.E.G. when last performed at the age of 16 months was normal.

Diagnosis: healthy.

Summary: a boy who had a possible head injury at the age of 5 months. This was followed by seizures and V.E.G. was performed at 8 months. Ratio was 0.33, 3rd ventricle 4 mm. Left side - 5 mm. Has developed normally and has no seizures.

168.

N.K. no. 01436/48. Boy born 19.5.47. No familial predisposition. Fourth of four children. Pregnancy and delivery normal. Birth weight 3750 g.

Symptoms: when a little more than 7 months old he had a sudden episode of pallor, clonic convulsions down the left side, loss of consciousness and frothing at the mouth which lasted one hour. Two days later there was a similar episode affecting the right side. Pneumonia was diagnosed. Six days later there was a further episode, on that occasion affecting both sides. He still had pneumonia and was admitted to hospital. There were two seizures 6 and 4 weeks before admission to the N.K. Department. X-ray of skull normal.

Admitted to N.K. department at the age of 10 months. Eyes normal. Neurological examination normal. X-ray of skull normal. Sub-dural puncture: no sign of hygroma.

V.E.G: pressure 150, clear fluid. Ratio on somewhat oblique projections: 0.34 (0.35/0.32). 3rd ventricle ? Right side - 12 mm. No complications.

Follow-up: was under State mental care and admitted to a special hospital at the age of 3 years. He died at the age of 3 years 4 months after a few hours' high fever. No autopsy.

Diagnosis: oligophrenia (idiocy), epilepsy.

Summary: a boy who began to have seizures at the age of 7 months. V.E.G. at 10 months showed a ratio of 0.34, right side - 12 mm. Placed under State mental care in a special hospital and died in hyperpyrexia of a few hours' duration.

169.

N.K. no. 08610/52. Boy born 1.10.47. Familial predisposition: older brother has affect convulsions. Father and father's brother had convulsions as children. Fourth of four

children. Pregnancy: no abnormality apart from nervousness. Birth normal. Birth weight 2400 g.

Symptoms: convulsion at the age of a year in connection with temper. Was unconscious for a short while and stiff in arms and legs. Admitted to hospital and from there transferred to convalescent home. Was seizure-free until a fright at the age of two years after which time he had generalised convulsions usually when he was tired. Petit mal seizures also occurred at that time. At the age of 4 years he had a convulsion of two hours' duration and was admitted to hospital. He had a high fever for several days and almost lost his speech afterwards. He was also partially paralysed in the arms and legs. Improvement was slow and arm movements were unsure. Admitted to the R.H. Neuro-medical Department. X-ray of skull: somewhat deep posterior fossa. E.E.G. and eye examination normal.

Admitted to N.K. department at the age of 4 years 3 months. Eye examination: blurring of the right disc nasally, probably not pathological. Voice rather hoarse. Appeared alert and in good general condition. Reflexes normal.

S.E.G.: pressure 300. Ratio 0.34 (0.32/0.36). 3rd ventricle 6 mm. Left side - 5 mm. Even distribution of surface air. No complications following the examination.

Follow-up: convulsions continued for two years after discharge but when the mother stopped going out to work there was a sudden improvement. On the recommendation of the school doctor and the invalid pension authorities the patient is in a hospital for epileptics but during admission there have been no real seizures. E.E.G. repeated on several occasions showed slight dysrhythmia with indication of left-sided preponderance. Neurological examination completely normal.

Diagnosis: epilepsy (very rare seizures).

Summary: a boy in whose paternal family there were convulsions. At the age of a year he had an affect convulsion and from the age of two years there were generalised convulsions and petit mal. S.E.G. at 4 years 3 months showed a ratio of 0.34, 3rd ventricle 6 mm. Left side - 5 mm. Seizures have almost ceased since the mother gave up work.

170.

N.K. no. 06797 a/51. Boy born 16.5.50. No known familial predisposition. Fourth of four children. Pyuria in pregnancy. Delivery normal. Birth weight 4150 g.

Symptoms: since the age of 2-3 months episodes of crying, becoming withdrawn, jerks in the arms and legs and colour change. Lasted 10-30 minutes and occurred 2-3 times a day. Admitted to the R.H. Paediatric Department at the age of 3 months. A quiet, withdrawn child with frequent small jerks. E.E.G.: no epileptic formations. Eye examination normal. X-ray of skull normal. Repeated blood sugar estimations showed low levels.

Admitted to N.K. department at the age of 5 months. Physical development corresponded to age. Head circumference 43 cm. The seizures appeared to be hypoglycaemic. E.E.G. normal.

S.E.G.: pressure 300, clear fluid. There was severe cortical atrophy primarily over the left hemisphere. Ventricular system was less well filled Ratio 0.35 (0.36/0.33). 3rd ventricle ? Right side - 13 mm.

Second admission to N.K. department at the age of 8 months. He had been at home for a few days but otherwise had been in R.H. Paediatric Department where exploratory laparotomy had been performed and no adenoma found. There was a right-sided hemiplegia present, more pronounced in the arm. Physical examination: head circumference 45 cm. Reflexes: no definite abnormality.

V.E.G.: pressure 100. Pronounced cortical atrophy over the right hemisphere. Ratio 0.37 (0.36/0.38). 3rd ventricle 9 mm. Left side - 17 mm. No rise in temperature or other complications after the examination.

Follow-up: died at the age of 10 months after admission to hospital because of otitis media. Autopsy diagnosis: bronchopneumonia, left-sided empyema, slight internal hydrocephalus, cerebral oedema and hyperaemia, infant brain with delayed development.

Diagnosis: epilepsy, right-sided spastic hemiplegia.

Summary: a boy who since the age of 2-3 months had seizures frequently connected with a low blood sugar. S.E.G. at 5 months showed a ratio of 0.35, right side - 13 mm.

Severe cortical atrophy on the left side. Exploratory laparotomy to exclude adenoma was negative. V.E.G. at 8 months showed a ratio of 0.37, 3rd ventricle 9 mm., left side - 17 mm. with cortical air over the right hemisphere. He died at the age of 10 months from bronchopneumonia.

171.

N.K. no. 06588/50. Boy born 21. 1. 45. No familial predisposition. Third of three children. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: when almost 5 years old he sustained a head injury when he fell and hit the crown of his head. This was followed 15 minutes later by seizures, loss of consciousness and jerks in all extremities, more pronounced on the right side. A subsequent right-sided hemiparesis disappeared over the next 24 hours. During the six months before admission he was somewhat irritable, obstinate, teasing and restless. Gait became unsteady and during the two months before admission there were 50 seizures with speech difficulty, vomiting, loss of consciousness and generalised spasms. E.E.G. as an out-patient at the age of 5 years showed no definite abnormality.

Admitted to N.K. department at the age of 5 years 10 months. Eye examination normal. Slight right-sided dysmetria and dysdiadokokinesis. All deep tendon reflexes missing or weak. Normal plantar reflexes. X-ray of skull: deep posterior fossa.

V.E.G.: attempted but had to be given up because of bleeding. Temperature 38.4° C. No complaints. Repeated V.E.G.: pressure 330. Ratio 0.35 (0.35/0.34). 3rd ventricle 5 mm. Left side - 7 mm. Normal surface air. Temperature 37.9° C. the second day, otherwise no complications.

Follow-up: had an occasional seizure after discharge but was then free until the age of 11 years when after a head injury unaccompanied by loss of consciousness or vomiting he had a generalised convulsion the same night which lasted two hours. Anti-epileptic treatment was then resumed. There was no decrease of function of the right side with that seizure. He can read well but is not so good at arithmetic. May possibly have had occasional seizures at night since the last generalised convulsion. Tires easily and often has a headache. Stammers a great deal. Physical examination: head circumference 55.5 cm. Eyes normal. Arm reflexes brisk but presumably not pathological. No abnormality in the legs. Balance good. Negative Romberg. Finger-nose and finger-finger test normal. Mentally appeared completely normal.

Diagnosis: epilepsy (long free interval between the two last seizures), stammer.

Summary: a boy who developed seizures and a transitory hemiparesis after a head injury at the age of 5 years. V.E.G. showed a ratio of 0.35, 3rd ventricle 5 mm., left side - 7 mm. He was seizure-free after discharge until another head injury after which he had a generalised convulsion. He is doing well at school and physical examination revealed no abnormality.

172.

N.K. no. 06673/50. Girl born 11. 7. 42. No familial predisposition. Second of four children. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: numerous attacks of otitis since early infancy and at the age of 6 years bilateral operations performed. Subsequent treatment was by syringing and radium. At the age of 5½ she banged her head in her sleep and at about the same time generalised convulsions of 2-3 minutes' duration were noticed. Further seizures occurred at irregular intervals. There were speech difficulties and she attended a special school. Admitted to a children's hospital at the age of 8 years.

Admitted to N.K. department at the age of 8 years. Eye examination: astigmatism, alternating convergent squint. Hearing decreased on both sides. Head circumference 53 cm. Reflexes weak, normal plantar reflexes. X-ray of skull: rather deep posterior fossa. E.E.G.: severe dysrhythmia essentially localised to the right hemisphere.

S.E.G.: pressure 210, clear fluid. Ratio 0.35 (0.34/0.36). 3rd ventricle 5 mm. Right side - 10 mm. Temperature 38° C. the same day, otherwise no complaints.

Follow-up: was in a school convalescent home until the age of 13 years. Both before and after this she was in a special school. Repeated examinations showed that with

increasing age she had increasing difficulty in keeping up. I.Q. at 7 years was 89. She did not do well at school and talked and read very poorly. At home she is very hysterical and the father feels she is a borderline mental defective. The family realises that she must eventually be placed under mental care. Physical examination (school doctor's report): 14 cm. too short for her age. No neurological abnormality. Hearing poor. E.E.G. at 13 years was only slightly abnormal but suspicious of epilepsy; nothing focal.

Diagnosis: behaviour problems, slight mental inferiority, previous epilepsy.

Summary: a girl who from infancy had repeated ear infections. Injured her head at the age of 6½ years after which generalised convulsions occurred. S.E.G. at 8 years showed a ratio of 0.35, 3rd ventricle 5 mm, right side - 10 mm. Has not done well at school, has severe behaviour problems and is a borderline mental case.

173.

N.K. no. 21741a/54. Boy born 18.9.39. No familial predisposition. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: at the age of 7 years had a sore throat and pneumonia. He did not fully recover from this illness and developed double vision, headache, paresis and convulsions affecting the left arm and leg. When he was 8 years old he underwent an operation for a large abscess in the right hemisphere at home in Iceland. He was symptom-free for the next four years when he again had a mild, progressive paresis of the left arm and leg and tonic convulsions of a few minutes' duration. At the same time he became dull and disinterested in his surroundings.

Admitted to N.K. department at the age of 12½ years. The left hand was slightly paralysed. He was an alert, smiling and mentally normal boy. There was a well-healed scar in the right temporal region. Reflexes normal. X-ray showed only sequelae of operation.

Operation performed over an area of brain prolapse which protruded about 2 cm. above the surface. There was a rather deep meningo-cerebral scar and superiorly a few atrophic gyri. Microscopy: meningo-cerebral scar.

Second admission to N.K. department nearly two years later after slight paralysis of the left arm and tonic and clonic convulsions with flexion of the left elbow and fingers of 15-60 seconds' duration. Had had some difficulty in expressing himself and stammered increasingly. During the six months before the second admission there had been seizures of two types, one the type already mentioned and the other characterised by strange sensations over the right side of the head. Two weeks before admission there had been unexplained fever. Physical examination revealed right-sided myopia and slight left-sided spastic hemiplegia, mostly in the arm. X-ray showed sequelae of craniotomy only. E.E.G. was severely abnormal with focal changes in the right temporo-central region.

S.E.G.: pressure 160, clear fluid. The pictures were not really measurable. There was definite dilatation, most pronounced on the right side and a ratio of approximately 0.35. 3rd ventricle 12 mm. Right side - 10 mm. Increased surface air was present on both sides. Temperature 38.2° C. the day after the examination. Otherwise no complaints.

Follow-up: family doctor in Iceland wrote to say that the physical development had proceeded normally but the left spastic hemiplegia was unchanged. Seizures continued and speech was very dysarthric. Every now and then he appeared rather unintelligent. However, he had attended school and taken the leaving examination so that reduction of intellectual ability could not be very great.

Diagnosis: left spastic hemiplegia, epilepsy.

Summary: a boy who after an infection developed seizures and hemiplegia and was operated on at the age of 8 years for a large abscess in the right hemisphere. At the age of 12 years he again developed seizures. Operation revealed a meningo-cerebral scar. Because of an increasing number of seizures S.E.G. was performed at the age of 14½, ratio approximately 0.35, 3rd ventricle 12 mm. Right side - 10 mm. He finished school, but continues to have seizures and a spastic hemiplegia.

174.

N.K. no. 00832a/47. Girl born 14. 12. 24. No familial predisposition. Fourth of six children. Pregnancy and delivery normal. Birth weight normal.

Symptoms: head injury in a cycling accident at the age of 9 years accompanied by loss of consciousness. Admitted to hospital where she had clonic convulsions down the left side. Craniotomy on the right side showed contused brain tissue down to the base with many bleeding points. Post-operative recovery uncomplicated apart from a few days' clonic jerks in the left facial area. For $3\frac{1}{2}$ years before admission there had been Jacksonian fits with loss of consciousness. They increased in frequency and a month before admission when they were at their worst they were occurring 5-6 times a day. The seizures were followed by paresis and hyperaesthesia in the left arm. There were also many hours' frontal headache. Admitted to the R.H. Neuromedical Department at the age of 12 years.

Admitted to N.K. department 3 months later. Eyes normal. Scar in the right temporal region. Slight left-sided central facial paresis. Fine nystagmus on looking to the left. Brisk left-sided patellar and Achilles tendon reflexes. X-ray of skull showed sequelae of craniotomy on the right side. L.E.G. unsuccessful.

V.E.G.: ratio 0.36 (0.37/0.34). 3rd ventricle 7 mm. Right side - 6 mm. Measurement not entirely accurate as it was made from reprints in the case records. Temperature 38.4° C. the day after, otherwise no complications.

Second admission to N.K. department at the age of 23 years. Seizures down left side with loss of consciousness and generalised convulsions. Was able to work but was rather slow. Admitted to the hospital for epileptics for a month at the age of 23.

L.E.G.: ratio 0.34 (0.37/0.32). Very thick left-sided cranial wall. Right side - 4 mm. Right-sided arteriography unsuccessful. On admission to N.K. department right-sided myopia found together with astigmatism. Mentally appeared rather clinging; epileptic. The patient did not wish any further examinations to be carried out. E.E.G. showed moderate dysrhythmia with diffuse changes.

Follow-up: re-admitted to hospital for epileptics, but now lives with her sister. E.E.G. showed severe dysrhythmia. Memory is increasingly poor and she is irritable and obstinate. There was pronounced distrust of the examiner and she refused almost all the examinations. Still has seizures. Mentally she appears to have given herself up and is rather depressed. Left-sided hemiparesis present, more pronounced in the arm. Receives an invalid pension because of intellectual difficulties.

Diagnosis: left-sided spastic hemiplegia, epilepsy, mental changes.

Summary: a girl who sustained a head injury at the age of 9 years. Craniotomy revealed contused brain tissue on the right side. Developed Jacksonian epilepsy. V.E.G. at 12 years showed a ratio of 0.36, 3rd ventricle 7 mm., right side - 6 mm. Examination repeated at 23 years showed a ratio of 0.34, right side - 4 mm. Still has seizures and a left-sided hemiparesis, is depressed and irritable.

175.

N.K. no. 07674b/51. Girl born 30. 7. 45. Familial predisposition: nil relevant. Sixth of seven children. Pregnancy normal. Birth 6 weeks premature. Birth weight 1500 g. Jaundice for the first 3-4 days of life.

Symptoms: four days before admission she fell from a table and hit the right side of her head. This was followed by numerous epileptic seizures lasting two minutes and a left-sided hemiparesis.

First admitted to N.K. department at the age of 2 years 10 months. Left arm and leg moved less well than the right. X-ray of skull normal. E.E.G. not done. Sub-dural puncture: fresh blood.

S.E.G.: pressure 110. Ratio 0.37 (0.37/0.37). Right side - 10 mm. 3rd ventricle ? Burr hole over the right hemisphere showed no abnormality. No rise in temperature or other complaints after the examination.

Second admission to N.K. department at the age of 5 years 2 months. Had been well until 6 weeks before admission when there had been an increasing number of seizures with loss of consciousness and convulsions in the left arm, occurring up to 4-5 times a

day and lasting two minutes. Eye examination normal. Left-sided spastic hemiplegia. X-ray of skull normal. E.E.G: severe dysrhythmia anteriorly with right-sided preponderance. S.E.G: ratio 0.47 (0.60/0.37). 3rd ventricle ? Right side - 16 mm. No complaints after the examination. Operation considered but parents were not willing.

Third admission to N.K. department at the age of 6 years. Daily generalised convulsions. Hemiparesis unchanged. Two weeks before admission she had had tonsillitis and had been feverish and tired for a week. The convulsions had increased in number and become more severe and the patient had become withdrawn and she cried now and then. On admission to a paediatric department pronounced neck stiffness was found and lumbar puncture showed elevated cell content. Pandy +++ positive. Spinal sugar 21 mg % and culture revealed tubercle bacilli. Treated with P.A.S., streptomycin and aureomycin. On admission to the N.K. department the child was withdrawn and had neck-stiffness. Head circumference 51 cm. and "cracked pot" sound on cranial percussion. Right pupil larger than the left. Left-sided spastic hemiplegia still present.

V.E.G: pressure 670, clear fluid. Ratio 0.55 (0.74/0.37). 3rd ventricle 16 mm. Right side - 8 mm. She had a high fever during the entire admission, deteriorated and died within a few days. Autopsy was not permitted.

Diagnosis: epilepsy, left-sided spastic hemiplegia, tuberculous meningitis.

Summary: a girl who was 6 weeks premature. When nearly 3 years old she sustained a head injury and had subsequent convulsions and left-sided hemiparesis. S.E.G. ratio 0.37, right side - 10 mm. When she was 5 years convulsions recommenced and increased. S.E.G. ratio 0.47, right side - 16 mm. During the final admission when she was 6 years old tuberculous meningitis was diagnosed and confirmed by culture of spinal fluid. V.E.G. ratio 0.55, 3rd ventricle 16 mm., right side - 8 mm. In spite of treatment she died.

176.

N.K. no. 22421/54. Boy born 5.11.51. No information on familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3700 g.

Symptoms: not very much known about the first year of life as he was in a children's nursery. Seen at the Blind Institute when almost 3 years old and atrophy of the optic nerve found. During the months prior to admission he had been restless and self-mutilating. Admitted to the R.H. Paediatric Department. L.E.G. revealed poor filling at the lower level of the third ventricle. Ratio 0.33 (0.32/0.34). 3rd ventricle 4 mm. Left side - 12 mm. No assessment of intelligence possible. E.E.G. normal. Head circumference 50 cm.

Admitted to N.K. department at the age of 2 years 9 months. Eyes: possible bilateral optic nerve atrophy. Bilateral nystagmus on looking to the left. Appeared severely retarded. X-ray of skull normal. E.E.G: no definite abnormality. Neurological examination normal.

V.E.G: pressure 100. Ratio 0.37 (0.39/0.35). 3rd ventricle 4 mm. Left side - 9 mm. Small amount of surface air. Temperature 38.4° C. the same day, normal on the third day. No other complications. Cortical biopsy showed no pathological changes.

Follow-up: admitted to a State mental institution at the age of 3 years. Was severely oligophrenic on admission, could only take fluids, had to be fed and was not toilet-trained. Movements very lively. I.Q. at 4 years impossible to assess. Has some vision and can understand something of what is said to him. Does not say anything himself, however. Physical examination: hid himself behind a towel. It was thought that he had some perception of light. He reacted violently when an attempt was made to persuade him to come out into the open. He still mutilates himself, particularly around the eyes. Patellar reflexes normal. Inconstant bilateral Babinski. Arm reflexes brisk but probably not pathological.

Diagnosis: oligophrenia (idiocy), sub-total blindness (atrophy of optic nerve).

Summary: a boy in whom atrophy of the optic nerves was established at the age of 3 years. Behaviour problems developed and L.E.G. showed a ratio of 0.33, 3rd ventricle 4 mm., left side - 12 mm. V.E.G. shortly afterwards showed a ratio of 0.37, 3rd ventricle 4 mm., left side - 9 mm. Placed in a State mental institution. Is very retarded and has severe behaviour problems. Has some perception of light.

177.

N.K. no. 1290/38. Girl born 17.1.29. No familial predisposition. Second of four children. Pregnancy and delivery normal. Birth weight 3250 g.

Symptoms: walked and talked rather late. Sustained a head injury at the age of 2 years and was unconscious for 12 hours. Convulsions followed and were accompanied by unconsciousness. They occurred at about monthly intervals and in between there were brief petit mal attacks. During admission to the R.H. Neuromedical department torsion spasms of the body and head and athetoid movements were seen together with marked mental retardation. The gait was ataxic.

Admitted to N.K. department at the age of 9 years 8 months. Physical examination: physical development that of an 8-year-old child, mentally very retarded, restless and crying. Legs somewhat rigid with brisk reflexes and patellar clonus. X-ray of skull: round skull with rather deep posterior fossa. Eye examination normal.

V.E.G.: pressure 75. Ratio 0.39 (0.40/0.38). 3rd ventricle 8 mm. Right side - 6 mm. Temperature 38° C. the same day, otherwise no complications.

Follow-up: patient has never been to school. It was the parent's impression that she became very much worse during her admission to hospital so they did not wish her to be admitted again. She helps at home and seems to have improved somewhat, particularly during the past two years. She still continues to have generalised convulsions. Physical examination: strong, heavy girl. Does not appear to have any endocrine disorder. Talks well, understands conversation and asks sensible questions. Head circumference 53.2 cm. Eye examination normal. Reflexes brisk, presumably not pathological. Normal plantar reflexes, no ankle clonus. Cannot stand on one leg and starts to cry immediately she is asked to do so. Mental development seems to be that of a 10-year-old or possibly a little younger. Never has febrile episodes.

Diagnosis: oligophrenia (debilitas mentis), epilepsy, obesity.

Summary: a girl whose development had been slow. Since a head injury at the age of two years convulsions, torsion spasms and athetoid movements. V.E.G. at 9 years 8 months showed a ratio of 0.39, 3rd ventricle 8 mm., right side - 6 mm. Lives at home. Intellectual development appears to be very retarded and she still has generalised convulsions. She is very over-weight.

178.

N.K. no. 3030/42. Boy born 23.4.39. No familial predisposition. Only child. Pregnancy normal. Birth prolonged and difficult. Moderate asphyxia. Birth weight 3200 g.

Symptoms: was ill from the first 24 hours of life and was admitted to hospital for three months. Was stiff and without power in all extremities, the legs and right arm being particularly affected.

Admitted to N.K. department at the age of 2 years 9 months. Appeared mentally retarded. Eyes: no definite abnormality apart from convergent squint. Severe spastic paresis, tetraplegia and muscular atrophy. Bilateral Babinski and brisk tendon reflexes. X-ray of skull: small, sutures almost closed.

V.E.G.: ratio 0.42 (0.43/0.41). Right side - 5 mm. 3rd ventricle 4 mm. Normal surface air. No complaints after the examination.

Follow-up: admitted to a State mental institution at the age of 4 years 8 months. *Diagnosis:* idiocy, spastic tetraplegia. Very poor condition. Seizures continued for a while but have ceased during the past year. No indication was found for treating his tetraplegia which is now very advanced and generalised muscular atrophy is also present. *I.E.G.:* at the age of 11 years showed a ratio of 0.45/0.47. 3rd ventricle not filled. Physical examination: very poor condition, does not say anything. Uses his arms and hands to some extent. Cannot raise himself up into a sitting position. Head circumference 53 cm. No squint. Legs cannot be used at all because of massive contractures.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia (legs more affected than arms), previous epilepsy.

Summary: a boy who had a difficult birth and was slightly asphyxiated. Rigidity was present from the first day of life. V.E.G. at 2 years 9 months showed a ratio of 0.42,

3rd ventricle 4 mm., right side - 5 mm. He is in a State mental institution, is very retarded and has a severe spastic tetraplegia.

179.

N.K. no. 00795/47. Boy born 15. 2. 47. No familial predisposition. Second of two children. Pregnancy normal. Delivery probably induced. Birth weight 3500-4000 g.

Symptoms: fell one metre at the age of 3 months without ill-effect. Developed high fever at the age of 7 months followed 5 days later by the first convulsion which lasted only a few seconds. They then increased in frequency, 6-7 times in a row at minute intervals in series 2-3 times a day. There was accompanying loss of consciousness. Six weeks before admission there was discharge from the left ear. Ceased to smile after the onset of the convulsions and showed no signs of recognising his parents. Admitted to a focus parieto-occipitally on the right. X-ray of skull normal.

Admitted to N.K. department at the age of 9 months. Eyes normal. Head circumference 49 cm., "cracked pot" sound on cranial percussion, more pronounced on the right side. Anxious looking child. X-ray of skull normal. Sub-dural puncture: clear fluid.

V.E.G.: pressure 50, ratio 0.43 (0.42/0.44). 3rd ventricle ? Right side - 8 mm. Temperature 38.3° C. the day after, otherwise no complaints.

Follow-up: convulsions continued after discharge and he was therefore re-admitted to hospital at the age of 18 months. Convulsions ceased when he had measles at the age of 3 years and he has had none since. Talked and walked at the normal time. Is in the appropriate school class for his age but has some slight difficulty with arithmetic. Investigated in a dermatology department because of a skin disorder on the face but no specific treatment was required. He is completely healthy and normally developed. Physical examination: healthy, normal appearance. Head circumference 54 cm. Eyes normal. Reflexes brisk but not pathological.

Diagnosis: healthy.

Summary: a boy who had a head injury at 3 months of age. When 7 months old he developed high fever and increasing convulsions. V.E.G. at 9 months showed a ratio of 0.43, right side - 8 mm. Convulsions ceased after he had measles at the age of 3. He is mentally and physically completely normal.

180.

N.K. no. 22535/54. Boy born 5. 3. 54. Familial predisposition: sister has congenital cataract. Second of two children. Pregnancy and delivery normal. Birth weight 2550 g.

Symptoms: squint and presumably decreased vision since birth. No neonatal jaundice. Development said to have been normal. Examined in the R.H. Eye Department and bilateral convergent squint found together with a somewhat irregular rotatory nystagmus. On ophthalmoscopy the discs appeared entirely normal. In the R.H. Paediatric Out-patient Department E.E.G. was performed and found to be severely abnormal with spike-focus parieto-occipitally on the right. X-ray of skull normal.

Admitted to N.K. department at the age of 6 months. Did not appear retarded and could follow light. Could not sit up. Eyes: atrophy of the optic nerve and convergent squint. Head circumference 44.5 cm. Doubtful "cracked pot" sound on cranial percussion. Babinski on the left and very brisk tendon reflexes in the left arm and leg.

V.E.G.: pressure between 200 and 300. Biopsy on the right side showed normal cortex on microscopy. Impression of severe hydrocephalus with only a few millimetres of preserved brain around.

V.E.G. repeated 5 days later. Again considerable dilatation, perhaps more severe on the right side. Large air-containing cyst on the right side, possibly old air from previous examination. Repeated for the third time 11 days later. Pressure on the right side 150. As before considerable porencephaly found particularly in the right frontal region. On none of the pictures could the ratio be measured accurately but it was probably about 0.40. There was an impression of severe dilatation and scattered porencephalies frontally and possibly also in the right hemisphere. No complications after the first examination. Temperature after the second was 40° C., and on the third day there was possibly slight neck-stiffness. There were no complications following the third examination.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Has a severe left-sided hemiplegia. Head circumference 52.5 cm. (at the age of 5 years). There is a squint and nystagmus on looking to the side. E.E.G. unchanged.

Diagnosis: left-sided hemiplegia (? triplegia).

Summary: a boy whose sister had a congenital cataract. He had a squint, nystagmus and decreased vision from birth. V.E.G. performed on three occasions at the age of 6 months showed a ratio approximately 0.40 and porencephaly primarily in the right frontal region. He now has a left-sided spastic hemiplegia, possible triplegia and continuing eye signs.

181.

N.K. no. 04170/47. Girl born 28.11.45. No known familial predisposition. Only child. No information about pregnancy. Delivery prolonged, 48 hours, and there was asphyxia. Birth weight unknown.

Symptoms: opisthotonus lasting about 30 seconds noticed at birth. Completely disinterested in surroundings.

Admitted to N.K. department at the age of 22 months. Eyes normal. Continuing tendency to opisthotonus. Tendon reflexes brisk. Bilateral Babinski. X-ray of skull: somewhat deep posterior fossa. E.E.G. not performed.

V.E.G.: pressure 100. Ratio 0.53 (0.52/0.53). 3rd ventricle large but not measurable. Right side - 6 mm. Increased surface air. Temperature 38.1° C. the day after, 39° C. on the fifth day, thereafter normal.

Follow-up: the patient was admitted to hospital at the age of two years and died three days later. She was extremely ill, emaciated and dehydrated and continued to have convulsions. Temperature 40.8° C. Autopsy diagnosis: cerebral atrophy, aspiration of stomach contents, internal and external hydrocephalus.

Diagnosis: severe oligophrenia, rigidity, epilepsy.

Summary: a girl whose birth was prolonged and who had asphyxia and opisthotonus. V.E.G. at 20 months showed a ratio of 0.53, right side - 6 mm. She died when aged two years with convulsions, high temperature, acute emaciation and dehydration.

182.

N.K. no. 08803/52. Boy born 1.4.51. No familial predisposition. Third of three children. No information available on pregnancy, delivery or birth weight.

Symptoms: when 7 months old developed high fever and was admitted to a hospital for infectious diseases. There rigidity, particularly of the legs, and a constant coarse tremor of the arms was found. Pneumococcal meningitis and acute bilateral suppurative otitis media diagnosed.

Admitted to N.K. department at the age of 11 months. Pronounced neck stiffness present. Head circumference 46 cm. Eyes normal. Did not appear retarded. Legs abducted at the hips and bent at the knees. Reflexes normal. X-ray of skull normal.

V.E.G.: pressure 230, clear fluid. Ratio 0.60 (0.59/0.61). 3rd ventricle 16 mm. Right side - 9 mm. There was some sub-dural air. Three days after V.E.G. there was leakage from the puncture site followed by vomiting. No leakage after the fifth day. Temperature 38° C. on the day of examination, normal by the third day.

Follow-up: patient has lived with his adoptive parents since the age of 3½ years. At that time he had adduction contractures, could not walk, hardly talked and was thought by most people to be mentally deficient. He has since made great progress, talks normally and goes to an ordinary kindergarten. I.Q. at the age of 7 years was 89. Physical examination: normal, healthy appearance. Intellectual development corresponds to age. Head circumference 54 cm. Eyes normal. There is a suggestion of bilateral ankle clonus but no Babinski. Patellar reflexes brisk but no extension of zones. Co-ordination and muscle tone normal.

Diagnosis: healthy (? intellectual inferiority).

Summary: a boy who had meningitis at the age of 7 months. V.E.G. at 11 months showed a ratio of 0.60, 3rd ventricle 16 mm., right side - 9 mm. Has developed normally since the age of 3½ years.

183.

N.K. no. 06056/50. Girl born 17.1.48. Familial predisposition: mother dull. A distant relative died in a State mental institution. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: would not take the breast. Possible head injury on the right side at the age of 4 months. Generalised convulsions began at the age of 8 months and lasted 4 hours. Admitted to hospital. Nystagmus and temperature of 38.5°C . found. Mental development retarded. Examined in the R.H. Paediatric Department and oligophrenia diagnosed.

Admitted to N.K. department at the age of 2 years 7 months because of new convulsions. Eyes: right-sided divergent squint. Head circumference 47 cm. Possible slight reduction of movement of the right arm and leg. E.E.G.: more low frequencies on the right than on the left.

S.E.G.: pressure 300, clear fluid. Poor ventricular filling.

S.E.G.: repeated: pressure 170, clear fluid. Ratio 0.63 (0.62/0.64). Right side - 5 mm. 3rd ventricle not measureable.

No complications following the first examination. Temperature 38.6°C . after the second.

Operation at the age of 2 years 8 months in the left pre-motor region. Numerous adhesions found and in addition a circumscribed atrophic brain lesion with microgyri and greyish-yellow colouring. There were many small sub-cortical cysts in the area. Microscopy: atrophic brain lesion with scar changes.

The morning after operation she collapsed and died. Autopsy diagnosis: localised microgyri following cortical atrophy, polyporencephaly, severe internal hydrocephalus.

Diagnosis: epilepsy, oligophrenia (imbecility), possible spastic hemiplegia.

Summary: a girl with a family history of mental retardation. Had a generalised convulsion at the age of 8 months and mental development was retarded. S.E.G. at 2 years 7 months showed a ratio of 0.63, right side - 5 mm. Operation in the left pre-motor region showed an atrophic lesion with scar formation. Died on the first post-operative day.

184.

N.K. no. 20422 a/53. Girl born 13.2.39. No familial predisposition. Third of five children. No information available on pregnancy, delivery or birth weight.

Symptoms: when 12 years old complained of pain behind the eyes and across the temples when reading, also possible blurred vision. Admitted to hospital in Iceland for investigation of possible intra-cranial tumour.

Admitted to N.K. department at the age of 13 years. Papilloedema of four dioptries. Neurological examination normal. X-ray of skull showed it to be large and thin-walled. Scattered digital markings, particularly in the anterior half of the sinus. E.E.G.: borderline abnormality in the right occipital region.

V.E.G.: pressure 340. Ratio 0.24 (0.28/0.23). 3rd ventricle 3 mm. Right side - 26 mm.

Operation over the right Sylvian fissure. Large sub-dural haematoma found which macroscopically appeared to be 6-12 months old, together with thick membrane extending over the whole left hemisphere. Anteriorly in the Sylvian fissure there was a cyst with clear fluid communicating with the chiasma cistern. The cyst was separated from the haematoma and opened, and the haematoma removed. Microscopic examination of the cyst: sequelae of chronic arachnoiditis with haemorrhage. Examination of the haematoma showed old and new haemorrhages. Post-operatively there was fever and a week after operation an abscess in the anterior part of the scar was opened. Almost three weeks later, because of continuing discharge and fever excision of infective granulation tissue.

Second admission to N.K. department at the age of 14 years. The patient had been completely well since operation and was admitted on this occasion for plastic surgery. Eyes: slight optic nerve atrophy. Neurological examination normal. X-ray of skull showed sequelae of craniotomy only. E.E.G.: moderately abnormal with low frequency focus over the left temporal region.

Plastic repair operation performed over the defect. Uncomplicated post-operative recovery.

Follow-up: family doctor in Iceland reported that the patient was in the best of health. She had developed completely normally and had no complaints.

Diagnosis: healthy.

Summary: a girl who at the age of 12 years had symptoms of increased intracranial pressure. V.E.G. ratio 0.24, 3rd ventricle 3 mm., right side—26 mm. Operation on the left side showed haematoma membranes and cyst formation. Re-admitted for plastic surgery the following year. Is completely well.

185.

N.K. no. 23200/55. Girl born 29. 10. 45. Familial predisposition: mother's father died at the age of 40 and mother's sister at the age of 3 years from inflammation of the brain. First of three children. Pregnancy and delivery normal. Birth weight 3340 g.

Symptoms: otitis media at 18 months which recurred at 3 years. At the age of 6 years admitted to hospital because of meningoencephalitis. Started school late. Generalised convulsion occurred at the age of 9½ followed by reduced power in the right-sided extremities.

Admitted to N.K. department at 9½ years. Appeared rather dull. Right-sided spastic hemiplegia present. Eyes: disc stasis, ? degree. X-ray of skull normal. E.E.G. severely abnormal with diffuse changes and focal low frequency activity in the left fronto-temporal region.

V.E.G.: pressure on the right side 300. Ratio 0.24 (0.22/0.26). 3rd ventricle 2 mm. Left side—9 mm. No complications.

Arteriography on the left side showed slight displacement to the left of both anterior cerebral arteries. Right-sided arteriography normal.

Follow-up: only occasional seizures now, and at examination there had been a seizure-free interval of 18 months. Attends a special school. Physical examination: head circumference 54.5 cm. Eyes normal. Reflexes: definite ankle clonus on the right, doubtful on the left. Brisk patellar reflexes, no Babinski. Tendon reflexes very brisk in the right arm.

Diagnosis: intellectual inferiority, grand mal (rare), slight degree of right-sided spastic hemiplegia.

Summary: a girl who had encephalitis at the age of 6 years. Generalised convulsions began at 9½ years with consequent reduction of power down the right side. V.E.G. ratio 0.24, 3rd ventricle 2 mm., left side—9 mm. Very rare seizures now. Still has slight degree of right-sided spastic hemiplegia. Attends a special school.

186.

N.K. no. 02346/48. Girl born 1. 2. 44. No information on familial predisposition. Pregnancy normal. Birth 4 weeks premature. No difficulty. Birth weight 2750 g.

Symptoms: at the age of 3 years 9 months fell off a chair. No vomiting or loss of consciousness. Two weeks later developed muscular spasms on one side of the mouth. No loss of consciousness but was very tired afterwards. Three weeks later there was a similar episode, lasting 4–5 minutes. At the age of 4 years the spasms recurred and she was admitted to hospital. On that occasion there was loss of consciousness. E.E.G. at 4 years 3 months showed no definite abnormality. X-ray of skull normal. Ten days before admission to N.K. department there were increasing muscular spasms round the mouth.

Admitted to N.K. department at 4 years 7 months. Eyes normal. X-ray of skull: increased digital markings, otherwise normal. Neurological examination normal. E.E.G. not done.

S.E.G.: pressure 120, clear fluid. Ratio 0.25 (0.23/0.27). 3rd ventricle 3 mm. No cortical atrophy. Temperature 38.2° C. Normal the next day.

Follow-up: shortly after discharge there were two seizures resembling the earlier ones but none since. Goes to school. Is left-handed but also uses right hand. Previously stammered a great deal. Mental development normal. Physical examination: head cir-

cumference 53 cm. Eyes and neurological examination normal. Normal, healthy appearance.

Diagnosis: healthy.

Summary: a girl who developed muscular spasms round the mouth two weeks after a head injury. They increased in number and were accompanied by loss of consciousness. S.E.G. at 4½ showed a ratio of 0.25, 3rd ventricle 3 mm. Apart from two seizures shortly after discharge, she has been completely well since.

187.

N.K. no. 06638/50. Girl born 1. 8. 46. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: fracture of the left temporal bone at the age of a year. Clonic convulsions and loss of consciousness at the age of two years while on the toilet. Four similar episodes during the next few days. Admitted to hospital at the age of 3 years 2 months after 7-8 new seizures. Further 3 seizures a year later. E.E.G. when 3 years old showed no definite abnormality. Repeated a year later when it showed moderate dysrhythmia.

Admitted to N.K. department at the age of 4 years 4 months. Eyes and neurological examination normal. Mental development also normal. X-ray of skull normal. E.E.G: moderate dysrhythmia with particularly low frequencies of high amplitude.

S.E.G: pressure 350, clear fluid. Ratio 0.26 (0.28/0.24). 3rd ventricle 5 mm. Even distribution of surface air. Temperature 38° C. the same day, normal the next day.

Follow-up: has been completely well since discharge. No seizures. Is in school class corresponding to her age. Physical examination completely normal.

Diagnosis: healthy.

Summary: a girl who sustained a fractured skull at the age of a year which was followed a year later by clonic convulsions and eventual loss of consciousness. S.E.G. at 4 years 4 months showed a ratio of 0.26, 3rd ventricle 5 mm. Completely well since discharge.

188.

N.K. no. 02635a/48. Girl born 4. 11. 40. No known familial predisposition. First of four children. Pregnancy and delivery normal. Birth weight about 3500 g.

Symptoms: severe head injury at the age of 2-3 years but no loss of consciousness. The day before admission the patient may have incurred another head injury while playing as a small abraison on the left side of the forehead was noticed. During play she became paralysed in the right leg and down the right side of the face, later also the right arm. Was confused and there was expressive aphasia.

First admission to N.K. department at the age of 6 years 7 months. Was withdrawn, sleepy at times and had expressive aphasia. ? momentary left divergent squint. Right-sided hemiparesis and peripheral facial paresis. Ophthalmoscopy showed no abnormality: X-ray of skull normal. E.E.G: generalised severe dysrhythmia. Sub-occipital puncture: pressure 90, clear fluid. Left sided arteriography: raising of anterior part of Sylvian vessels. During the next few days the patient began to talk again but the right-sided hemiplegia remained. Two weeks after admission V.E.G. performed.

V.E.G: pressure 60. Ratio 0.22 (0.19/0.25). 3rd ventricle 4 mm. Temperature 38.4° C.

Operation over the left hemisphere: the cortex appeared normal but there was abnormal vessel distribution in that the vessels were collected together in star formation. No haematoma. Hemiplegia unchanged on discharge.

Second admission to N.K. department when nearly 8 years old. The patient had had physiotherapy at another hospital and at the age of 7 years had had special boots and splints fitted at the Orthopaedic Hospital. The foot had improved but not the arm and she was re-admitted for this reason. Talked normally. The right arm hung flaccidly with the hand flexed. Reflexes brisker on the right side than on the left. Loss of sensation on the right side. Eyes normal. E.E.G: reduced dominant frequency with increase of low frequencies, mostly on the right side. Left-sided arteriography: slightly irregular progress of the media cerebral artery. Clear filling of the anterior cerebral artery.

S.E.G.: ratio 0.26 (0.23/0.29). 3rd ventricle 5 mm. Left side - 11 mm. Temperature 38.2° C. the same day, otherwise no complications.

Follow-up: right-sided spastic hemiplegia treated by physiotherapy. Did well at school. At the age of 15 she had an uncomplicated rheumatic fever and was admitted to hospital. She is a girl guide and plays handball. Walks and runs and does not tire any more easily than other children. Physical examination: head circumference 55.4 cm. Eyes normal. Right-sided facial paresis. Speech normal. Severe right-sided hemiplegia, more pronounced in the arm. This is atrophic and the hand is held in a typical cerebral palsy position. Tendon reflexes brisk on both sides, but more on the right. Legs: ankle clonus on the right together with Babinski. Patellar reflexes elicited from whole tibia. Abduction of hips to 140°. Intelligence appears normal.

Diagnosis: right-sided spastic hemiplegia.

Summary: a girl who at 2-3 years of age had a severe head injury and a possible further injury when 6½ accompanied by right-sided paralysis. *V.E.G.* ratio 0.22, 3rd ventricle 4 mm. Operation over the left hemisphere showed some slight vessel abnormalities. *S.E.G.* when nearly 8 years old showed a ratio of 0.26, 3rd ventricle 5 mm., left side - 11 mm. At follow-up the right-sided spastic hemiplegia was unchanged. Mental development was normal.

189.

N.K. no. 03162/49. Girl born 1.8.45. No familial predisposition. First of two children. Pregnancy normal. Delivery fast and uncomplicated. Birth weight about 3000 g.

Symptoms: when the patient was about 6 months old it was noticed that she could not use her right hand and arm and later the right foot did not function normally. Investigated at the Orthopaedic Hospital.

Admitted to N.K. department at the age of 3½ years. Eyes normal. Head circumference 49 cm. Right-sided spastic hemiplegia. X-ray of skull: coarse closely packed digital markings occipitally. *E.E.G.*: dominant frequency depressed frontally on the left side.

V.E.G.: pressure 250, clear fluid. Ratio 0.26 (0.22/0.31). 3rd ventricle 3 mm. Temperature 38.5° C. the same day, otherwise no complications.

Right-sided arteriography: normal.

Follow-up: investigated at a children's hospital at the age of 6 years. *E.E.G.* showed continuing dysrhythmia and moderate asymmetry, right side less abnormal than the left. Treatment at Orthopaedic Hospital has been completed with better results in the leg than in the arm. Never has seizures. Is doing well at school, can sew and knit but almost always uses left hand. Physical examination: healthy, normal appearance. Mental state normal. Right spastic hemiplegia present. No eye signs.

Diagnosis: right-sided spastic hemiplegia.

Summary: a girl who was found to have a right-sided spastic hemiplegia at the age of 6 months. *V.E.G.* at 3½ showed a ratio of 0.26, 3rd ventricle 3 mm. Hemiplegia has improved to some degree and she is doing well.

190.

N.K. no. 08517/52. Boy born 10.1.43. Familial predisposition: mother's sister is in a mental hospital. Mother's cousin attended a special class. Second of two children. Pregnancy: in bed during the 2nd-3rd month because of haemorrhage. Delivery normal. Birth weight 3500 g.

Symptoms: the child's toxoplasmosis reaction was weak positive with a dye test titre of 1-50 and complement fixation titre 1-4. Mother also had a weak positive reaction. The child was always retarded in development. There were two minor head injuries in early childhood without obvious ill-effects. Toilet trained at 4 years. In the year or so before admission there had been behaviour problems. Admitted to a children's hospital at the age of 8 years 10 months. *E.E.G.* showed moderate dysrhythmia. I.Q. 52.

Admitted to N.K. department at the age of 9 years. Eyes normal. Speech inarticulate. X-ray of skull: slightly square head with a few digital markings. *E.E.G.*: focal dysrhythmia with a focus in the left temporal region.

S.E.G.: pressure 200, clear fluid. Ratio 0.26 (0.23/0.29). Left side - 5 mm. 3rd ventricle 7 mm. Surface air evenly distributed. Temperature 38.1° C. the same day.

Follow-up: was for a while in a special school. I.Q. at 5 years 62, 14 years 45. Is now in a State mental institution. Physical examination: speech is very poor. He is left-handed. No neurological signs.

Diagnosis: oligophrenia (imbecility), dysarthria.

Summary: a boy with a family history of mental disorder. Mother bled during pregnancy and both she and her child had weak positive toxoplasmosis reactions. He was retarded and had behaviour difficulties. *S.E.G.* at 9 years showed a ratio of 0.26, left side - 5 mm. Is in a State mental institution.

191.

N.K. no. 08814b/52. Boy born 13.4.45. Familial predisposition: older brother born deaf. Second of two children. Pregnancy and delivery normal. Birth weight 3250 g.

First admission to N.K. department at the age of 3 years via a Casualty Department after falling from a first floor window with subsequent loss of consciousness. *Operation* revealed a depressed fracture over the left hemisphere with a 10 cm. long lesion in the dura and a deep laceration through the hemisphere. Only the definitely necrotic tissue was removed.

Second admission to N.K. department 3 months later for plastic surgery. The patient had continued to improve and needed only slight support when walking. On both admissions his temperature rose, to 38° C. post-operatively. There were no other complications.

Third admission to N.K. department at the age of 7 years. Speech had improved and the paresis had disappeared. Admitted because of progressive hearing difficulty which was confirmed by otological examination and a hearing-aid was recommended. Physical examination: possible right-sided optic nerve atrophy. Left-handed. Slight reduction of power in the right arm and leg. *E.E.G.*: severe focal dysrhythmia over the left occipito-parietal region. X-ray of skull normal apart from sequelae of earlier operation.

S.E.G.: pressure 200, clear fluid. Ratio 0.27 (0.23/0.31). 3rd ventricle ? Left side - 6 mm. Normal surface air. No post-examination reaction.

Follow-up: has done well since discharge and has had no convulsions. Was for a time at a special school because of his deafness together with his brother who is still there. Then attended a normal school and now goes to school at the Speech Institute. He has not shown much interest at school because of his hearing difficulties. I.Q. in an ordinary examination is slightly under average but at a later assessment when his deafness was taken into consideration he was found to be above average intelligence. Motor ability entirely normal. Physical examination: on examination at the Speech Institute the patient appeared extremely bright and alert. According to the teacher he is aphasic and word-blind. Reflexes normal. Head circumference 57 cm. Eyes normal.

Diagnosis: aphasia (familial deafness?), word-blindness.

Summary: a boy whose brother was born deaf. At the age of 3 years he sustained a depressed skull fracture. Due to progressive loss of hearing *S.E.G.* was performed when he was almost 7 years. This showed a ratio of 0.27, left side - 6 mm. He is now in the Speech Institute and has normal intelligence. He appeared to be aphasic and word-blind.

192.

N.K. no. 06711a/51. Boy born 30.1.41. No known familial predisposition. First of two children. Pregnancy: oedema towards the end of the period. Father died at that time. Delivery was difficult, caudate position. Birth weight 5040 g. The child was very sick for the first few days but then improved spontaneously. No jaundice.

Symptoms: generalised teething convulsions at the age of two years. At just about that time fell from a ground floor window. Did not lose consciousness but vomited. Admitted to hospital for a week. Was then symptom-free until the day of his ninth birthday when he had a generalised convulsion that lasted three-quarters of an hour. This was followed by another convulsion six months later and during the interval there

had been episodes of petit mal. Admitted to a hospital for epileptics at the age of 9 years. He slowed down intellectually. I.Q. 66. E.E.G: dysrhythmia anteriorly on the left side as well as in the left temporal region.

L.E.G: ratio 0.31 (0.27/0.34). 3rd ventricle 5 mm. Right side - 18 mm.

Admitted to N.K. department at the age of 9 years 9 months. Co-operated poorly and seemed dull. Eyes normal. Possible reduction of power in the left arm. Reflexes: abnormal on the left side. X-ray of skull: long and narrow skull with close digital markings. Dorsum sellae showed early atrophy. Left-sided arteriography: poor pictures and a tumour could not be excluded.

S.E.G: pressure 100, clear fluid. Pictures showed displacement to the right but could not be measured. 3rd ventricle 4 mm.

V.E.G: pressure 105. Pictures as before. From a frontal picture one gained the impression that the left lateral ventricle was the largest. 3rd ventricle 4 mm.

Operation on the left side revealed normal cortex.

Operation on the right side: dura adherent to the arachnoid. Frontally in the temporal region there was pronounced atrophic involvement and the cortex was only a few millimetres thick. The anterior part of the lobe was removed. Microscopy showed a traumatic brain lesion.

Second admission to N.K. department when nearly 11 years old because of leakage of fluid and fever. Eyes showed possible early disc protrusion.

S.E.G: ratio 0.27 (0.20/0.34). 3rd ventricle 8 mm. Right side - 10 mm. After removal of pus from between the bone and the dura *S.E.G.* repeated.

S.E.G: pressure 280. Ratio 0.33 (0.32/0.34). Right side - 19 mm. 3rd ventricle difficult to measure, ? 12 mm. There was severe headache after both *S.E.G.* and *V.E.G.* After first examinations temperature rose to 38.1°C . and after the second series to 38.8°C . He was febrile during most of the second admission.

Follow-up: he was in the hospital for epileptics before his admission to the N.K. department, also between admissions and for a short while after discharge. Has since been well. Has a hearing-aid but does not seem to need it. Has left school and works for a plumber. Never has convulsions and only occasionally has a headache. Memory is completely normal. Physical examination: mental development normal. Head circumference 53.2 cm. Reflexes normal. Eyes normal.

Diagnosis: healthy.

Summary: a boy who had a difficult birth. Had teething convulsions at two years of age and at about that time sustained a head injury. No seizures until age of 9 years when he had a generalised convulsion which was repeated 6 months later. *L.E.G.* ratio 0.31, 3rd ventricle 5 mm., right side - 18 mm. Operation on right side revealed an atrophic lesion in the temporal lobe. Repeated *S.E.G.* at age of 11 years showed a ratio of 0.33, right side - 19 mm. He is now doing well. Has a slight loss of hearing but this does not bother him.

193.

N.K. no. 08472/51. Boy born 27. 3. 51. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3600 g.

Symptoms: 4 days after birth there was diarrhoea followed two days later by fever. Admitted 3 weeks after birth to the R.H. Paediatric Department with swinging temperature, usually above 38°C . E.E.G. normal. X-ray of skull and eye examination normal. The major sign was flaccidity.

Admitted to N.K. department at the age of 9 months. Eyes normal. Head circumference 43.5 cm. Very flaccid, did not hold head up and could not sit or stand. E.E.G. normal.

S.E.G: pressure 400, clear fluid. Ratio 0.27 (0.24/0.31). Increased cortical air on the left side. 3rd ventricle 6 mm. Temperature was raised before the examination, 40.4°C . the same day. No other complaints.

Follow-up: developmental quotient at the age of 3 years 45. Followed up as an out-patient and admitted for two months at the age of 5 years for intestinal investigation when enteritis was established. Petit mal attacks noted during admission. Said single words, and mostly used signs and sounds. E.E.G. continued to be severely abnormal. He gave

the impression of being one of the "non-talkers, non-jumpers". There was slight spastic paraplegia. At the later examination there were no definite reflex changes.

Diagnosis: oligophrenia (imbecility), epilepsy, possible cerebral palsy ("non-talker, non-jumper" syndrome).

Summary: a boy who developed diarrhoea and fever and accompanying flaccidity soon after birth. S.E.G. at 9 months showed a ratio of 0.27, 3rd ventricle 6 mm. Petit mal seizures noted at the age of 5 years. Appears to be a "non-talker, non-jumper" and is mentally retarded.

194.

N.K. no. 20633/53. Boy born 24. 2. 48. No familial predisposition. Third of four children. Pregnancy and delivery normal. Birth weight 4400 g.

Symptoms: after a "blister" on the eardrum at the age of 10 months he was rigid and almost paralysed down the right half of the body. Treated by physiotherapy from the age of two years. From the age of 3½ years he had 5 long-lasting convulsions which were generalised but predominantly right-sided and he was admitted to a children's hospital. Development not retarded but speech not very clear.

Admitted to N.K. department at the age of 5 years 2 months. Could say only single words. Head circumference 52 cm. Eyes normal. Otological examination normal. Slight left-sided facial paresis and right-sided spastic hemiplegia. Right-sided Babinski and brisk tendon reflexes. E.E.G.: severely abnormal with spikes localised to the left hemisphere. X-ray of skull normal.

S.E.G.: pressure 170. Ratio 0.27 (0.24/0.32). 3rd ventricle ? Surface air on the left side. Left side - 7 mm. No rise in temperature or other complications.

Follow-up: admitted to a hospital for epileptics at the age of 5 years 4 months where he stayed for six months. Diagnosed as a case of epilepsy, right-sided spastic hemiplegia, intellectual inferiority. Has since been in a home for epileptics. I.Q. at the age of 7 years 64. Goes to school but probably does not learn much. Is very spiteful. Has occasional petit mal attacks and at the age of 8 years had a number of generalised convulsions. He takes anti-epileptic drugs. Physical examination: head circumference 52.5 cm. Right-sided spastic hemiplegia, particularly affecting the arm. He can dress himself and is toilet-trained. There is an intermittent squint but no nystagmus. Speech is good.

Diagnosis: right-sided spastic hemiplegia, epilepsy, oligophrenia (debilitas mentis).

Summary: a boy who after an ear infection at the age of 10 months developed a right-sided spastic hemiplegia and convulsions at the age of 3½ years. S.E.G. ratio 0.27. Left side - 7 mm. He is in a home for chronic epileptics and continues to have a right-sided spastic hemiplegia. I.Q. is 64.

195.

N.K. no. 03683/49. Girl born 8. 7. 38. No familial predisposition. Only child. Pregnancy and delivery normal. Slight birth marks were present. Birth weight 3500 g.

Symptoms: when 9 years old she hit the back of her head and was momentarily unconscious. Several days later she complained of headache localised to the back of the head accompanied by dizziness and vomiting. Headaches were particularly troublesome when she was tired. She appeared now and then to be rather withdrawn and seemed a little dull. Did well at school, however. After the injury there appeared to be a gradual reduction of hearing, especially on the left side.

Admitted to N.K. department at the age of 10 years 10 months. Neurological examination normal. Healthy, normal appearance. Otological examination: bone conduction deafness and suggestion of perception disturbance. One could not be certain whether or not the acoustic nerve as well as the middle ear was involved. X-ray of skull normal. E.E.G.: some slow activity chiefly posteriorly and to the right.

S.E.G.: pressure 150, clear fluid. Ratio 0.29 (0.24/0.34). 3rd ventricle 2 mm. Normal distribution of surface air. Temperature 38.4° C. the day after and slight headache. Otherwise no complication. Attempt at arteriography was abandoned because the patient became transiently aphasic and developed a right-sided spastic paresis chiefly involving the arm.

Follow-up: has developed normally. Has taken the school leaving examination and again complained for a while of tired eyes and headache. Menarche occurred without trouble. Was tested for vocational ability and found to be considerably above average in everything except where bodily strength and speed were required. Physical and mental state normal. No seizures. Hearing still reduced on the left.

Diagnosis: left-sided deafness, healthy.

Summary: a girl who at 9 years of age had a head injury followed by headache and left-sided hearing loss. S.E.G. at that time showed a ratio of 0.29, 3rd ventricle 2 mm. She developed normally and was of above average intelligence. Hearing loss still present on the left side.

196.

N.K. no. 02477/48. Boy born 26. 2. 47. No familial predisposition. First of two children. Pregnancy normal. Delivery easy but patient was asphyxiated. Birth weight 3250 g.

Symptoms: admitted to a paediatric department for 3 weeks immediately after birth because of cyanosis and frothing at the mouth. Blood-stained spinal fluid found. Development was slow and at the age of 7-8 months paresis of the right arm was noticed. When about 18 months old he had his first seizure which first affected the right arm and later also the left side with accompanying loss of consciousness. Admitted to the R.H. Paediatric Department. X-ray of skull: noticeably large, otherwise no definite abnormality.

Admitted to N.K. department at the age of 19 months. Eyes normal. Tendon reflexes brisker on the right than on the left side. No Babinski. Right-sided hemiparesis. E.E.G. not done.

S.E.G.: clear fluid. Ratio 0.34 (0.19/0.50). 3rd ventricle 6 mm. Left side - 6 mm. Temperature 39° C. the day after, normal on the third day. No other complications.

Follow-up: has done well since. Followed up for a while as an out-patient at the R.H. Paediatric Department and later in an orthopaedic out-patient department. Has not had seizures for many years. E.E.G. at the age of 5 years showed moderately severe dysrhythmia with fast activity over the left hemisphere. Physical examination: head circumference 52 cm. Eyes normal. Intelligence appears normal. Patient has a right-sided hemiplegia, involving the arm more than the leg.

Diagnosis: right-sided spastic hemiplegia.

Summary: a boy who was asphyxiated at birth and had signs of intracranial haemorrhage. Paresis of the right arm was noticed at the age of 7 months and convulsions occurred at 18 months. S.E.G. at that time showed a ratio of 0.34, 3rd ventricle 6 mm., left side - 6 mm. He has done well since, attends an ordinary school and has no seizures.

197.

N.K. no. 06003/50. Boy born 20. 7. 44. Familial predisposition: an older brother is mentally retarded. Second of two children. Pregnancy and birth normal but the child nevertheless did not cry until 5-10 minutes after delivery. Birth weight 2750 g.

Symptoms: was very sleepy for the first 14 days. At the age of 6 months he cried a great deal and was very restless. Convulsions affecting the left half of the face and the left arm and leg began at 2 years of age. He began to walk at the age of 3 years and decreased power in the left leg was noticed. Began to talk at the age of 5 years.

Admitted to N.K. department at the age of 6 years. Eyes: convergent squint. Left-sided hemiplegia present. X-ray of skull: medium sized skull, thin-walled with increased digital markings. E.E.G: severe dysrhythmia.

V.E.G.: pressure 120, clear fluid. Ratio 0.36 (0.21/0.50). 3rd ventricle 5 mm. Left side - 12 mm. No rise in temperature or other complications following the examination. Burr hole made in the right pre-motor region some days later showed normal cortex.

Follow-up: examined at the Orthopaedic Hospital's cerebral palsy clinic and in the R.H. Paediatric Out-patient Department. Moderate left-sided hemiplegia present which is improving under treatment. He is oligophrenic, says only a few words but understands what is said to him. He is at home under State mental care. He has generalised convul-

sions and E.E.G. is severely abnormal with spike focus in the right fronto-temporal region.

Diagnosis: left-sided spastic hemiplegia, epilepsy, oligophrenia (? debilitas mentis).

Summary: a boy whose brother is mentally retarded. Crying was delayed at birth and he was very sleepy. From the age of 2 years had convulsions involving the left side of the body. Development was delayed and V.E.G. at 6 years showed a ratio of 0.36, 3rd ventricle 5 mm., left side - 12 mm. Is under State mental care at home and continues to have convulsions and a left-sided hemiplegia.

198.

N.K. no. 07361/51. Boy born 11. 11. 48. Familial predisposition: father's brother had epilepsy until the age of 11 years. Mother's mother had epilepsy. Third of three children. Pregnancy and delivery normal. Birth weight 3370 g.

Symptoms: fell twice when about 9 months old without immediate ill-effects. Soon after, however, minor seizures began during which his head fell forward. The seizures increased until they were occurring 20 times a day. Stood at 2 years and walked shortly after. The child could not talk on admission to hospital. During the six months prior to admission he had not been on anti-epileptic treatment but had only had threatened seizures. Admitted to a children's hospital at the age of one year and again at two years. E.E.G.: severe dysrhythmia of hypsarrhythmic type. X-ray of skull normal. Developmental quotient 54.

Admitted to N.K. department at the age of 2½ years. Eyes normal. Head circumference 50 cm. Appeared an imbecile. Gait unsteady and broad-based. Reflexes normal. X-ray of skull normal.

S.E.G: pressure 110, clear fluid. Ratio 0.28 (0.25/0.33). 3rd ventricle 6 mm. No complications after the examination.

Follow-up: followed up in the out-patient department of a children's hospital. Continues to take anti-epileptic drugs and still has occasional minor seizures when his head falls forward. E.E.G. at the age of 7 years was considerably better and there were only very occasional abnormal findings during sleep. Developmental quotient at the age of 4 years 61 and at 5 years 83. Attends a private school. Physical examination: normal, healthy appearance. Motor system normal. Reflexes normal. During the examination he had a petit mal attack. Does not appear mentally retarded. Is left-handed.

Diagnosis: epilepsy with hypsarrhythmic type of E.E.G. Possible slight reduction of intelligence (I. Q. 54, → 83, → ?).

Summary: a boy with epilepsy in the family. Shortly after a couple of minor head injuries at the age of 9 months he began to have minor seizures during which his head fell forward. He was late walking and talking. S.E.G. ratio was 0.28, 3rd ventricle 6 mm. Has improved considerably, especially intellectually. He has almost no seizures and no motor handicap.

199.

N.K. no. 05428/50. Girl born 27. 11. 48. No familial predisposition. Second of two children. No information on pregnancy. Birth 6 weeks premature. No asphyxia. Birth weight 2000 g.

Symptoms: was always too quiet and slept and dozed a lot. Weight gain was poor and she could not walk at 18 months.

Admitted to N.K. department at the age of 17 months. Eyes normal. Head circumference 43 cm. Could sit and stand for a short while without support. Reflexes normal. X-ray of skull normal. E.E.G. not done.

S.E.G: pressure 250, clear fluid. Ratio 0.29 (0.25/0.33). 3rd ventricle 4 mm. No complications after the examination.

Follow-up: it has been impossible to contact the patient because she has been away at each attempt. Her own doctor has written to say that mental and physical development are retarded and there is a slight right-sided spastic mono- or hemiplegia including the facial nerve. Speech is poor. She has no convulsions but there is a tendency to febrile episodes, tonsillitis and otitis.

Diagnosis: right-sided spastic mono- or hemiplegia, dysarthria, intellectual inferiority.

Summary: a girl who was 6 weeks premature and whose development was slow. S.E.G. at 18 months showed a ratio of 0.29, 3rd ventricle 4 mm. At follow-up she had a spastic mono- or hemiplegia on the right side, was mentally retarded and had speech difficulties.

200.

N.K. no. 22746/54. Boy born 19. 10. 54. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3000 g.

Symptoms: was increasingly ill when 5-6 days old and was admitted at the age of 12 days because of loss of weight, vomiting and diarrhoea. No convulsions. Infantile diarrhoea, colitype 26 was diagnosed. His head grew $2\frac{1}{2}$ cm. in 10 days, the sutures gaped and the fontanelles bulged. Eyes normal. X-ray of skull: gaping sutures.

Admitted to N.K. department at the age of a month. Eyes normal. Head circumference 38 cm. Bilateral Babinski and brisk patellar reflexes. Sub-dural puncture showed no signs of hygroma.

S.E.G.: pressure 200, clear fluid. Ratio 0.29 (0.25/0.32). 3rd ventricle 2 mm. Increased surface air over the right hemisphere, particularly corresponding to the insular area. No temperature or other complications.

Follow-up: has developed normally and is clever. E.E.G. at 7 months was normal. Physical examination: alert child whose abilities correspond to age. Speech normal. Head circumference 53 cm. Reflexes normal. Neurological examination normal.

Diagnosis: healthy.

Summary: a boy who during the first weeks of life had epidemic diarrhoea and a rapid increase in head circumference. S.E.G. at one month showed a ratio of 0.29, 3rd ventricle 2 mm. Is now completely healthy.

201.

N.K. no. 1927/40. Girl born 21. 5. 31. No familial predisposition. Sixth of seven children. Pregnancy: poorly for most of the time with frequent vomiting. Delivery difficult with breech presentation. Birth weight 3000-3500 g. No neonatal symptoms.

Symptoms: generalised convulsions of unknown origin occurred at the age of 9 months. She was then symptom-free until the age of 8 years when she had a Jacksonian seizure localised to the left side of the face and later affecting the arm. The seizures increased in number and she complained of headache. Continued to do well at school.

Admitted to N.K. department at the age of 9 years. Eyes normal. Slight right-sided facial nerve paresis. Reflexes otherwise normal. Arteriography: no definite abnormality.

V.E.G.: normal pressure. Ratio 0.31 (0.28/0.35). 3rd ventricle 5 mm. Normal surface air. Temperature 39° C. the same day, otherwise no complications.

Follow-up: has had no seizures since discharge. Is somewhat nervous and now and then has slight pressure headache over the right side. No dizziness or eye symptoms. Has had many jobs and done well in them. Is 6 months pregnant and is completely well. Physical examination: healthy, normal appearance. Head circumference 59 cm. Eyes, reflexes and motor system normal.

Diagnosis: headache, healthy.

Summary: a girl who had a difficult delivery by breech presentation. Generalised convulsion occurred at 9 months and from the age of 8 years there were Jacksonian seizures affecting the left side of the face and the arm. V.E.G. when nearly 9 years old showed a ratio of 0.31, 3rd ventricle 5 mm. Has had no seizures since and apart from an occasional headache she is very well.

202.

N.K. no. 9247a/47. Boy born 15.12.32. No known familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight 3000 g.

Symptoms: head injury at the age of 3 years but no loss of consciousness or other symptoms. When 4 years old he had an unexplained episode of 3 weeks' fever without obvious involvement of the central nervous system. Petit mal began at the age of 8 years and there was a single episode of tonic convulsions in all extremities.

Admitted to N.K. department when almost 14 years old. Eyes: pupils unequal size. Neurological examination normal. X-ray of skull normal. E.E.G: severely diffuse dysrhythmia.

S.E.G: on two occasions: pressure 140. Pictures technically not very good. Ratio 0.32 (0.27/0.36). 3rd ventricle 5 mm. Temperature 38.4° C. after examination.

Second admission to N.K. department at the age of 15 years when a tumour could not be excluded and *V.E.G.* was performed. Pressure 80, clear fluid. Tumour was excluded. Ratio as before 0.33 (0.29/0.37). 3rd ventricle? Temperature was 38.2° C. for a few days. Otherwise no complications.

Follow-up: admitted to a hospital for epileptics many times for long periods at a time, the longest from the age of 16–20 years and again at the age of 23. Only occasional seizures during admission, usually petit mal. Has been trained as a bookbinder and since discharge has been followed up as an out-patient. E.E.G. still shows some dysrhythmia. I.Q. 78 ± 4. Physical examination: mentally appears to be rather slow and clinging. Speech is good. Head circumference 58 cm. Eyes and reflexes normal.

Diagnosis: epilepsy, intellectual inferiority.

Summary: a boy who at the age of 4 years had an unexplained febrile episode. Petit mal began at 8 years and there was a single tonic convulsion. S.E.G. when nearly 14 years showed a ratio of 0.33. Has spent most of his time in a hospital for epileptics and has an I.Q. of approximately 80.

203.

N.K. no. 05545c/50. Boy born 2. 11. 44. No familial predisposition. Only child. Pregnancy normal. Delivery difficult with asphyxia lasting 20 minutes. Birth weight 2900 g.

Symptoms: would not take the breast. Development normal. Walked at a year and was toilet trained at 2½. Christmas Eve, 1948, when he was 4 years old he had a brief seizure with jerks of the right hand. Admitted to the R.H. Paediatric Department.

Admitted to N.K. department at the age of 4 years 4 months. Eye, neurological and psychological examination normal.

S.E.G: pressure 180, clear fluid. Ratio 0.32 (0.29/0.36). 3rd ventricle 2 mm. Was slow waking up after the anaesthetic and flaccid and dull the next morning. Otherwise no complications.

Further admissions were because of seizures. E.E.G. showed severe localised dysrhythmia on the left side on two occasions. At the age of 5½ left-sided arteriography was performed and showed no abnormality. No rise of temperature or other complications.

Follow-up: has since been examined as an out-patient in the R.H. Paediatric Department. I.Q. 98. Goes to school. E.E.G. shows a severely abnormal curve with spike focus in the left temporo-parietal region. He continues to have brief seizures at monthly intervals. These affect the right eye and right side of the mouth. He is conscious but cannot speak until 15 minutes after the attack. Neurological examination normal. Head circumference 55.3 cm.

Diagnosis: epilepsy.

Summary: a boy who was asphyxiated at birth for 20 minutes. Localised seizure at the age of 4 years. S.E.G. ratio 0.32, 3rd ventricle 2 mm. Arteriography at 5½ was normal. Has developed normally but continues to have seizures at monthly intervals.

204.

N.K. no. 09550a/52. Boy born 16. 11. 43. No familial predisposition. Second of two children. Pregnancy normal. Delivery full-term, severe. No asphyxia. Birth weight 4000 g.

Symptoms: during the first 6 months of life had repeated otitis and bronchitis. The day before admission he fell backwards out of his high-chair and hit the back of his head. There was no loss of consciousness but an hour later he perspired and became withdrawn and this was followed three hours later by convulsions.

Admitted to N.K. department at the age of 16 months. Continued to have tonic spasms of the right side of the face and right arm. Eyes deviated to the right and there was rhythmic nystagmus on looking to the left. X-ray of skull normal.

V.E.G: ventricles normally placed but small and compressed. Temperature 40.3° C.

the day after the examination. On discharge there was slight paresis of the right-sided extremities.

Second admission to N.K. department at the age of 8 years 9 months. Mental development normal but he stammered a great deal. On day of admission was hit by a wooden ball on the left side of the head and $1\frac{1}{2}$ hours later legs became flaccid. Three hours later he lost consciousness and developed clonic jerks in the right hand and round the mouth. Convulsions then became generalised. Physical examination: deviation of gaze to the left, otherwise no abnormality on eye examination. Right-sided spastic hemiplegia present. Cisternal puncture: pressure 80, clear fluid. X-ray of skull normal. E.E.G. showed severe dysrhythmia with low frequency activity over the left hemisphere, particularly posteriorly. Left-sided arteriography: somewhat bow-shaped formation of anterior cerebral artery.

S.E.G. pressure 180, clear fluid. Ratio 0.32 (0.36/0.27). 3rd ventricle 5 mm. No complications following the examination.

Follow-up: some weeks after the second admission to the N.K. Department the convulsions recurred and a year later petit mal began. Mysoline treatment was started and he was then seizure-free. He has had many problems at school and has been partly in a private school, partly in a boarding school and most recently in a day school. He is word-blind and periodically stammers. Lately there have been seizures beginning with spitting and salivation and followed by stiffness of the right hand. The seizures are short and the patient is unaware of them himself. He has also had two episodes of unconsciousness and generalised convulsions immediately after injections. He has been admitted to the R.H. Paediatric Department where E.E.G. was shown to be severely abnormal with focus in the left temporal region. The moderate right-sided hemiplegia continues but is now almost confined to the arm alone. I.Q. about 85.

Diagnosis: right-sided spastic hemiplegia, epilepsy.

Summary: a boy who had a difficult delivery. After an injury at 16 months he developed convulsions. V.E.G. showed small ventricles. After another head injury at the age of almost 9 years he was unconscious and had convulsions. S.E.G. at that time showed a ratio of 0.32, 3rd ventricle 5 mm. Continues to have seizures which more resembled petit mal and still has a slight right-sided hemiplegia. Has some school problems.

205.

N.K. no. 21231/53. Boy born 4.10.50. No relevant familial predisposition. Only child. Pregnancy normal. Delivery induced, otherwise normal. Birth weight 3500 g.

Symptoms: two years before admission fell from pram without apparent ill-effect. When almost 3 years old had two generalised convulsions with loss of consciousness and stammered slightly afterwards. Three hours before admission had a left-sided convulsion beginning in the arm and with loss of consciousness. Admitted to hospital where a left-sided hemiparesis was found.

Admitted to N.K. department at 2 years 11 months. Eyes normal. Head circumference 49 cm. Slight left-sided hemiparesis and Babinski. X-ray of skull normal. E.E.G. severely abnormal with low-frequency activity particularly over the right hemisphere fronto-temporally.

S.E.G. pressure 350, clear fluid. Ratio 0.32 (0.36/0.29). 3rd ventricle 4 mm. Temperature 38.4° C. the day after examination and slight headache. Otherwise no complications.

Right-sided arteriography showed normal conditions.

Follow-up: has had no convulsions since admission but occasionally complains of headache. Motor system normal. Understanding is good. Can now and then be somewhat hot-tempered. The mother thinks that he is somewhat immature with regard to obedience etc. Physical examination: head circumference 51.5 cm. Speech normal. Eye and neurological examination normal. Mental development appears to correspond to age.

Diagnosis: headache, previous epilepsy, healthy.

Summary: a boy who sustained a head injury when about 11 months old and at 2 years 11 months developed generalised convulsions. S.E.G. showed a ratio of 0.32, 3rd ventricle 4 mm. Completely normal at follow-up apart from occasional headaches.

206.

N.K. no. 23292/55. Girl born 24. 3. 54. No familial predisposition. Only child. Pregnancy: mother fell 14 days before delivery. Delivery: patient was asphyxiated for 20 minutes. Birth weight 2750 g.

Symptoms: admitted immediately after birth because of tonic convulsions. Jaundiced from the 3rd to 10th day of life. Very flaccid after discharge but had no convulsions, though there was an episode when breathing stopped. Retardation suspected at the age of 4 weeks and she was re-admitted to the R.H. Paediatric department. E.E.G. at 9 months showed a tendency to patchy depression of activity on the left side. Eye examination: possible atrophy of the optic nerve, alternating convergent squint. Petit mal seizures seen during admission.

Admitted to N.K. department at the age of 14 months. Did not react to light and probably not to sound. Eyes: unco-ordinated movements. Appeared flaccid without increased muscle tone. Bilateral Babinski.

V.E.G.: cortex appeared macroscopically normal. After burr holes had been made pulse and respiration stopped and examination was discontinued. It was repeated five days later: pressure 75, heavily bloodstained fluid from a new haemorrhage. Ratio 0.32 (0.29/0.35). 3rd ventricle 6 mm. Normal distribution of cortical air. No complications after the second examination.

Follow-up: patient is at home and attends the R.H. Paediatric Department for follow-up. Physical examination: head microcephalic, 48.5 cm. at 4 years. Eyes: nystagmus and squint. Severe spastic tetraplegia and corresponding reflex changes. Mental development somewhat retarded.

Diagnosis: oligophrenia (imbecility?), spastic tetraplegia, epilepsy.

Summary: a girl who was asphyxiated for 20 minutes and immediately after birth had tonic convulsions. Retarded development suspected at 4 weeks. V.E.G. at 14 months showed a ratio of 0.32, 3rd ventricle 6 mm. Is at home, has severe mental retardation and spastic tetraplegia.

207.

N.K. no. 07685/51. Girl born 12. 5. 50. No familial predisposition. Only child. Pregnancy normal. Delivery by forceps with asphyxia. Birth weight 3100 g.

Symptoms: during the first week of life there were many cyanotic attacks accompanied by generalised convulsions. These gradually ceased. At the age of 10 months it was noticed that the patient would not stand on her right leg and on admission to hospital a right-sided hemiplegia was found.

Admitted to N.K. department at the age of 14 months. Eyes normal. Right-sided spastic hemiplegia. Head circumference 44.5 cm. X-ray of skull normal.

S.E.G.: pressure 300, clear fluid. Ratio 0.33 (0.30/0.36). 3rd ventricle 7 mm. Some surface air particularly over the left frontal region. No temperature or other complications after the examination.

Follow-up: continues to be followed up in the R.H. Paediatric Department. She has a right-sided spastic hemiplegia and attends a special school. I.Q. at the age of 9 years was 75 which is the same as at previous examinations.

Diagnosis: right-sided spastic hemiplegia, intellectual inferiority.

Summary: a girl whose delivery was by forceps and who was asphyxiated. Convulsions occurred during the first week of life. Spastic hemiplegia on the right side noticed at 10 months. S.E.G. at 14 months showed a ratio of 0.33, 3rd ventricle 7 mm. Is under treatment for spastic hemiplegia and attends a special school. I.Q. approximately 75.

208.

N.K. no. 23519a/55. Boy born 30.4.42. No familial predisposition. Second of two children. Pregnancy normal. Delivery difficult and child said to be asphyxiated. Birth weight 3400 g.

Symptoms: cyanotic and dull for the first 8 days. Thereafter no symptoms until the age of 5 months when he had a seizure affecting the left leg. Similar seizures followed

and he was therefore admitted to hospital. Mental and physical development very retarded. Admitted to R.H. Paediatric Department at the age of a year because of seizures and a paresis varying from side to side was found. There was also slight ptosis of the left upper eyelid. Admitted to the R.H. Neuromedical Department at the age of 2 1/4.

Admitted to N.K. department at the same age.

V.E.G: pressure 100. Ratio 0.34 (0.39/0.27). 3rd ventricle not definitely filled. Normal surface air. Temperature 38.9° C. for the first five days after examination.

Follow-up: re-admitted to the R.H. Paediatric Department at the age of 4 years. Some progress, could talk but could not walk. Severely mentally retarded. Generalised hypotonia present. Re-admitted at age of 6 years. Fewer seizures but tendency to cyanosis. Condition characterised by hyperkinesia. Last admitted to the R.H. Paediatric Department at 10 years 8 months. X-ray of skull normal. E.E.G. showed no definite abnormality. I.Q. 36. Admitted to a State mental institution when nearly 12 years old. Diagnosed as a case of imbecility, hydrocephalus, lipothymia, hereditary familial paralysis, basal ganglia lesion, leucoencephalopathy. Had to be helped to dress. He said that he had had a transitory paresis but there was no sign of this on examination. Second admission to N.K. department at the age of 13 years 3 months. The patient could not read, write or count. There was bilateral Steward-Holmes' sign. He appeared somewhat ataxic. E.E.G: severely abnormal with low frequency activity, ? slight abnormality in the left hemisphere. S.E.G: pressure 370, clear fluid. Ratio 0.35 (0.39/0.31), 3rd ventricle 4 mm. Increased basal air. Temperature 38.2° C. for two days, otherwise no complications. After the examination in the N.K. Department he improved considerably, became stronger and was only occasionally troubled by his paresis. Physical examination: head circumference 54 cm. Physically no abnormality to be seen.

Diagnosis: oligophrenia (imbecility), possible periodic familial paresis.

Summary: a boy with a difficult delivery and possible asphyxia. Seizures started at the age of 5 months and he was found to be mentally and physically retarded. At the age of a year an alternating paresis was found together with slight ptosis of the left upper eyelid. V.E.G. at 2 1/4 showed a ratio of 0.34. Placed in a State mental institution at the age of 12 years. I.Q. 36. S.E.G. at the age of 13 years 3 months showed a ratio 0.35, 3rd ventricle 4 mm. Has made some progress since the last examination.

209.

N.K. no. 06940e/51. Girl born 21. 3. 42. No familial predisposition. Second of two children. Pregnancy and birth normal. Birth weight 3250 g.

Symptoms: convulsions since birth and paresis of left arm and leg since age of 4 days. Admitted to hospital. Since the age of a year generalised convulsions with loss of consciousness. Began to walk at 2 years but gait rather hesitant. Began to talk at 2 years.

First admission to N.K. department when nearly 3 years old. Pale, thin child. Eyes: left convergent squint. Left-sided spastic hemiplegia, more pronounced in the arm. Left-sided tendon reflexes brisker than on the right. Left-sided Babinski. X-ray of skull normal.

S.E.G: pressure 200, ratio 0.34 (0.28/0.39). 3rd ventricle 9 mm. Normal surface air.

V.E.G: pressure 200. Conditions much the same as on S.E.G. No rise in temperature or other complications.

Second admission to N.K. department at the age of 7 years. Patient had been almost seizure-free until 3 weeks before admission when she sustained a head injury. Following that there were increasing left-sided convulsions in spite of increasing the anti-epileptic drug dosage. In behaviour she was irritable and contrary. Eye examination: atrophy of the optic nerve, convergent squint, nystagmus. E.E.G: severe dysrhythmia. Many epileptiform changes posteriorly and to the right.

Third admission to N.K. department 3 weeks after second because of convulsions. Discharged to a hospital for epileptics and readmitted a fourth time from the epileptic hospital having also been at home for a while. Convulsions continued in spite of treatment. Eyes: pallor of discs and atrophy, otherwise as at the last examination. Because of technical difficulties she was temporarily discharged and re-admitted a fifth time four months later. At that time the convulsions were gradually decreasing and had occurred only during the first month but petit mal had begun again. Eyes unchanged. Left-sided spastic hemi-

plegia present. Appeared very retarded and psycho-labile. Admitted sixth time to N.K. department at the age of 9 years when convulsions had again increased. Left-sided hemiplegia as before. Wide *craniotomy* performed on the right side. Greyish discolouration of the arachnoid particularly in the pre-motor region where there appeared to be some atrophy. Electroencephalography showed a focus in the post-central region. Excision and coagulation of this area performed. Microscopy: cortical tissue. No post-operative complications apart from a temperature of 38.8° C. the same day.

Follow-up: from the age of 10-13 years she was in a home for chronic epileptics. I.Q. at 9 years was 42. Placed under State mental care and attended a day school at the age of 13. Has a predominantly left-sided hemiplegia though the right side is also affected. Can talk and understands what is said to her. Behaviour is stereotyped. Gets on well with other children. E.E.G. at the age of 14 showed a severely abnormal curve with bilateral changes more pronounced on the right side. No seizures.

Diagnosis: oligophrenia (imbecility), left-sided spastic hemiplegia (or spastic tetraplegia, left side more affected than right).

Summary: a girl who had convulsions and a left-sided paresis from birth. S.E.G. at the age of almost 3 years showed a ratio of 0.34, 3rd ventricle 9 mm. Admitted repeatedly during the next year because of increasing seizures. Craniotomy performed at 9 years of age showed atrophy in the right pre-motor region. The atrophic area was removed. Is under State mental care and attends a special school. Has a predominantly left-sided spastic tetraplegia.

210.

N.K. no. 21128a/53. Boy born 18.2.41. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: injured his head when he fell out of bed at the age of 6 years. No loss of consciousness. At the age of 9-10 years began to have episodes of staring which were followed by headache. Occurred about 6 times a month. Did well at school. Admitted to the R.H. Paediatric Department at the age of 11 years 7 months. E.E.G: spike focus over the right occiput. L.E.G: severe dilatation of ventricular system.

First admission to N.K. department at 11 years 9 months. Head circumference 56 cm. Eyes and reflexes normal. X-ray of skull normal. E.E.G: severe dysrhythmia, spike-wave focus in the right occipital region.

S.E.G: pressure 150, clear fluid. Ratio 0.34 (0.30/0.37). 3rd ventricle 3 mm. Slight headache after examination and temperature of 39.1° C. Neck stiffness and a positive Kernig's sign also present. Rapidly disappeared.

Second admission to N.K. department 9 months later because of continuing seizures. Physical examination: no abnormality. No special investigations carried out.

Follow-up: has been working for the past six months in a factory and has had no seizures for two years though gets an occasional headache. Vocational testing showed that he was unsuitable for fine handwork but capable of manual work. Physical examination: head circumference 59 cm. Healthy, normal appearance. Eyes and neurological examination normal.

Diagnosis: healthy.

Summary: a boy who began to have seizures at the age of 9-10 years accompanied by headache. S.E.G. when nearly 12 showed a ratio of 0.34, 3rd ventricle 3 mm. No seizures after the age of 14 and only occasional headache. Is working and completely healthy.

211.

N.K. no. 00277/47. Boy born 18.6.42. Familial predisposition: an older sister has spastic paraplegia and a cousin's mother has disseminated sclerosis. Fourth of five children. Pregnancy: no information. Delivery normal. Birth weight normal.

Symptoms: hit by a swing at the age of 5 years and was unconscious for a short time. Two hours later there was disturbance of gait and loss of balance. Admitted to a hospital and from there to the R.H. Neuromedical Department. Bilateral Babinski and ataxic gait. Eyes and X-ray of skull normal.

Admitted to N.K. department two months later when there was bilateral dysidiado-kokinesis, uncertainty on knee-heel test, broad-based unsteady gait, brisk patellar reflexes, bilateral ankle clonus and bilateral Babinski.

V.E.G.: pressure 170, clear fluid. Ratio 0.35 (0.30/0.39). 3rd ventricle 5 mm. Temperature 38.2° C. the same day, normal on the third day. Otherwise no complications.

Follow-up: was referred to the Orthopaedic Hospital's cerebral palsy clinic at the age of 10 years. After the hospital admission at the age of 5 he had to learn to walk again. At the age of 7 years he had concussion with prolonged unconsciousness. Managed very well on a tricycle and went to a school for disabled children until the age of 10 after which he was admitted to the Orthopaedic Hospital's special school and later to a trade school. There was apparently no progression of the disability while he was there. His appearance is somewhat feminine but this is not very pronounced. E.E.G. at the age of 11 showed moderately diffuse dysrhythmia. I.Q. at 15 was 94. His gait has improved. Physical examination: at the age of 15 there was no abnormality of the cranial nerves. The arms were slightly hypotonic and there was some tremor and dysidiadokokinesis. Left side not so much affected as the right. Legs: moderate symmetrical spasticity with hyperactive reflexes and Babinski. Head circumference 54 cm.

Diagnosis: spastic paraplegia (familial).

Summary: a boy whose older sister has spastic paraplegia. At the age of 5 years he was hit by a swing which was followed two hours later by disturbance of gait and balance. V.E.G. ratio 0.35, 3rd ventricle 5 mm. Concussion at the age of 7 years with a long period of unconsciousness. Has been under special care and his gait has improved. Is doing fairly well at a trade school.

212.

N.K. no. 08120/51. Boy born 15. 6. 39. No familial predisposition. First of two children. Pregnancy normal. Delivery prolonged but no asphyxia. Birth weight about 3000 g.

Symptoms: when about 8 years old and again at 11 had repeated minor head injuries. At 11½ he had two episodes of jerks down the right side without loss of consciousness. Admitted to the R.H. Neuromedical Department at the age of 12 where E.E.G. showed possible changes in the left hemisphere. Left-sided arteriography: suspicion of temporal tumour. L.E.G. normal.

Admitted to N.K. department at 12 years. Physical examination: brisk reflexes. E.E.G. occasional discharges of high amplitude.

S.E.G.: pressure 150, clear fluid. Ratio 0.35 (0.32/0.38). 3rd ventricle 4 mm. Normal surface air. Temperature 37.9° C. the same day.

Follow-up: has developed completely normally both from a mental and physical point of view. Has occasional episodes of jerks in the right hand at very long intervals. Is now apprenticed to a plumber. Physical examination: normal, healthy appearance. Mental development normal. Head circumference 56 cm. Neurological examination normal.

Diagnosis: healthy.

Summary: a boy whose delivery was lengthy and who began to have spasmodic jerks down the right side of the body at the age of 11½ years. There had been a series of minor head injuries at the age of 8 and again at 11 years. S.E.G. ratio at 12 years was 0.35, 3rd ventricle 4 mm. Is doing well apprenticed to a plumber. Has very infrequent jerks in the right hand.

213.

N.K. no. 03200b/49. Girl born 6. 6. 35. No familial predisposition. Third of four children. No information on pregnancy. Delivery normal. Birth weight 3500 g.

Symptoms: admitted to hospital at the age of 9 months because of enteritis. Head injury occurred at 4 years followed by pallor and tiredness. Another head injury at the age of 7 years with pain over the parietal region and frontal headache for two weeks. Following this she had five episodes during which she became stiff and remote for a few seconds. Two months and again one month before admission had a convulsion affecting right arm and leg as well as the right side of the face and accompanied by loss of consciousness. The first convulsion lasted 1½ hours and the second an hour and both

were accompanied by faecal incontinence. Admitted to hospital at the age of 7 years. X-ray of skull and eye examination normal.

Admitted to N.K. department at 7 years 3 months. Eyes normal. X-ray of skull showed increased intracranial pressure. Neurological examination revealed no definite abnormality.

V.E.G.: pressure 90. Ratio 0.36 (0.33/0.39). 3rd ventricle 5 mm. Temperature 38.3° C. the next day, otherwise no complications.

Second admission to N.K. department at 11 years 2 months. Petit mal continued and the child was mischievous and difficult. Four months before admission she had had pneumonia and at the same time many convulsions followed by sudden right-sided hemiplegia. This improved and there were only residual changes in the arm. Physical examination: eyes normal. Pronounced spastic paresis of the right arm and slight right-sided facial paresis. E.E.G. showed moderately severe dysrhythmia.

S.E.G.: pressure 120. Ratio 0.39 (0.34/0.44). 3rd ventricle 8 mm. Temperature 39.6° C. the third day with neck stiffness. High fever for about 14 days.

Third admission to N.K. department at the age of 13 years 8 months. After discharge she had had weekly convulsions and these increased during the month before admission. The convulsions began in the right arm, lasted about 30 seconds and usually occurred during the morning. Physical examination: eyes normal. Slight right-sided spastic hemiplegia affecting the arm more than the leg. X-ray of skull: medium-sized, somewhat thin-walled. No definite abnormality. E.E.G. showed severe dysrhythmia. Mental state normal.

V.E.G.: ratio 0.56 (0.44/0.68).

Operation over central area of left hemisphere. Cortex showed atrophic changes but without real scar formation. E.E.G. showed a focus downwards over the media cerebral artery in the central area of the temporal lobe as well as upwards into the motor region. The upper part of the motor region contained a focus which was removed so that the lateral ventricle was opened wide. Microscopy showed contused brain tissue and ganglion cell degeneration and glia proliferation. There was post-operative paralysis of the right arm, high temperature and neck stiffness. Repeated puncture beneath the scar flap performed. E.E.G. and eye examination showed no change. On discharge the patient could walk with support but still had paresis of the right arm.

Follow-up: admitted for almost a year between the age of 16-17 to a hospital for epileptics. E.E.G. at that time showed moderately severe dysrhythmia with right-sided preponderance. Work was good but capacity below a third. L.E.G. at the age of 16 had shown the left side to be more dilated than the right and the dilatation was more pronounced than it had been in the N.K. Department. There were no good A-P pictures but sequelae of operation could be seen on the left side as well as increased air on the right side, in one of the pictures occupying about half the distance to the cranial wall. Readmitted to a hospital for epileptics at the age of 21 for vocational testing. She had been at home and had done well. Work had improved after treatment had been started with Largactil. Physical examination: head circumference 55.5 cm. Right-sided spastic hemiplegia affecting the arm more than the leg with corresponding reflex changes. Mental development almost corresponded to age. Speech was good and she could do handwork etc. but presumably not well enough to take a proper job.

Diagnosis: right-sided spastic hemiplegia, epilepsy, ? intellectual inferiority.

Summary: a girl who sustained head injuries at the age of 4 and 7 years and developed headache, petit mal and later localised right-sided seizures. V.E.G. at 7 years showed a ratio of 0.37, 3rd ventricle 5 mm. Because of increasing petit mal and a sudden right-sided hemiplegia S.E.G. was performed at the age of 11 and showed a ratio of 0.39, 3rd ventricle 8 mm. V.E.G. when almost 14 years showed a ratio of 0.56. Operation over the left hemisphere showed alteration in cortical tissue and this tissue was removed. She has a right-sided spastic hemiplegia and only rare seizures. Her intelligence is almost normal but she is presumably unable to work.

214.

N.K. no. 05012/50. Girl born 22.9.48. No familial predisposition. Only child. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: at the age of 16 months, 5 days before admission, she developed a temperature of 39.5°C . and generalised convulsions. Admitted to a paediatric department where she was found to be unconscious and having small spasms. Reason for fever was not found. Treated with antibiotics but when these were stopped temperature rose again and she had two further generalised convulsions.

Admitted to N.K. department at the age of 17 months. Eyes normal. Head circumference 50 cm. Single clonic jerks in the right side of the face and right arm. Babinski and brisk patellar reflexes on the right side with increased muscle tone. X-ray of skull: somewhat large with large posterior fossa. Possibly slightly increased digital markings. E.E.G.: low activity especially pronounced over the left hemisphere and anteriorly.

V.E.G.: pressure 120. Ratio 0.37 (0.32/0.41). 3rd ventricle 7 mm. Pronounced subdural air on the right side. None on the left. Temperature 38.8°C . the next day, normal on the third. No other complications.

Follow-up: has been completely well. On discharge she was paralysed down the right side but could walk again at the age of two years. Attends a normal school and is doing well. Arithmetic is her best subject. Prefers to use left hand. Has no seizures. Physical examination: mental development normal. Head circumference 53 cm. Eyes normal. Ankle clonus and Babinski on the right side. Brisk patellar reflexes but no extended areas. Reflexes in right arm brisker than in left. No reduction of function. Right hand and arm held somewhat awkwardly when running but can be used.

Diagnosis: slight right-sided spastic hemiplegia.

Summary: a girl who at 16 months has generalised febrile convulsions. V.E.G. at that time showed a ratio of 0.37, 3rd ventricle 7 mm. Has been well since, has no seizures and attends a normal school. Physical examination showed a slight spastic right-sided hemiplegia.

215.

N.K. no. 05309/50. Girl born 10. 10. 48. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: convulsion at the age of 5 months in connection with high fever. Admitted to a paediatric department. The first two convulsions were generalised and the third left-sided. Otitis media was found and pneumococci type 19 cultured. Spinal fluid contained 76/3 cells. There were two further episodes of febrile convulsions. Nothing was found clinically but E.E.G. showed a focus posteriorly in the right hemisphere.

Admitted to N.K. department at the age of 17 months. Eyes normal. Head circumference 48 cm. Could support herself but not walk. Seemed to understand. Reflexes normal. X-ray of skull normal. E.E.G.: severe dysrhythmia more pronounced posteriorly on the left side.

S.E.G.: pressure 230, clear fluid. Ratio 0.37 (0.34/0.40). 3rd ventricle not filled. Surface air corresponded to the left Sylvian fissure. Temperature 38.1°C . the day after, normal on the second day. Otherwise no complications.

Follow-up: continued to have febrile convulsions until she was 2 years old. Anti-epileptic treatment was continued until the age of about 5 years and she has had no seizures since. Walked at 13 months and talked at the normal time. On follow-up the patient attends a normal school and is doing well, particularly at arithmetic. Physical examination: physical and mental development corresponds to age. Seemed to be severely upset by the examination and it had to be abandoned. Eyes normal.

Diagnosis: healthy, affect reaction.

Summary: a girl who had febrile convulsions at the age of 5 months and again later. S.E.G. at 17 months showed a ratio of 0.37, 3rd ventricle not filled. At follow-up febrile convulsions had continued until the age of two years but she has since been perfectly well.

216.

N.K. no. 21157/53. Girl born 24. i. 50. No familial predisposition. First of three children. Pregnancy: 3-4 days' bleeding during the 4th-5th month and vomiting. Delivery full-term but difficult. The child was fed for two hours. Birth weight 3000 g. There was a slight degree of neonatal jaundice.

Symptoms: slow development. At the age of 6 months violent trembling of head and hands was noticed. Admitted to R.H. Neuromedical Department at the age of two years. L.E.G. showed surface air. Diagnosis: possible cerebellar ataxia. Violent trembling recurred and she was therefore re-admitted. Diagnosed as cerebellar ataxia. L.E.G. normal. Ratio 0.30 (0.30/0.30). 3rd ventricle 3 mm. Since treated as an out-patient in the R.H. Paediatric Department. E.E.G. at the age of 3 years showed severe focal dysrhythmia with spike focus over the left temporal region.

Admitted to N.K. department at the age of 3 years 9 months. Eyes: partial paralysis of eye movements on the right together with nystagmus. Possible right-sided convergent squint. Understood requests and smiled. Physical development retarded. Could not sit, stand or walk Generalised hypotonia with increased left-sided patellar reflexes, athetoid movements and intention tremor.

V.E.G.: pressure 0, clear fluid. Ratio 0.38 (0.34/0.43). 3rd ventricle 11 mm. Large cortical air collection. Patient was feverish before, during and after the examination. Biopsy from occipital cortex showed severe ganglion cell degeneration and possible congenital dysplasia.

Follow-up: admitted many times to a paediatric department. Last admitted at the age of 4 years because of fever. During admission she had continuous small spasms especially in the face. Improved on Mysoline treatment. When nearly 5 years old she developed secretory stagnation in the upper respiratory tract and high fever and died. Autopsy diagnosis: patchy bronchopneumonia, acute mucopurulent tracheobronchitis, degeneration of hepatic parenchyma, acute hyperplasia of spleen, encephalitis and cerebral oedema.

Diagnosis: ataxia, athetosis, epilepsy.

Summary: a girl who had a difficult delivery. Over the next 6 months there was increasing trembling of the whole body. V.E.G. showed a ratio of 0.38, 3rd ventricle 11 mm. Cortical biopsy showed possible congenital dysplasia. Continued to have fibrillations and died from acute febrile tracheobronchitis at the age of 4 years.

217.

N.K. no. 22449/54. Boy born 2.3.54. No familial predisposition. Only child. Pregnancy: vomiting but no other complications. Delivery normal. Birth weight 3300 g.

Symptoms: examined in the R.H. Paediatric Out-patient Department at the age of one month because of restlessness thought to be due to possible inadequacy of breast milk. At the age of 4 months had repeated infantile spasms which came at variable intervals and lasted a few seconds. Often occurred in series of 3-4 jerks and many times in an hour. Admitted to the R.H. Paediatric Department at the age of 5 months. X-ray of skull normal. E.E.G. severely abnormal with spikes of right-sided predominance, hypsarrhythmic type.

Admitted to N.K. department at the age of 6 months. Eyes: ? blind. Head circumference 41 cm. Muscle tone increased particularly in the legs. Bilateral Babinski. E.E.G. not done. Motor and mental development retarded. Could not hold his head up, sit or grip. Did not recognise his parents.

V.E.G.: pressure 110, ratio 0.39 (0.34/0.44). 3rd ventricle 11 mm. Temperature 39.4° C. the day after, normal on the fourth day. Otherwise no complications.

Follow-up: admitted to the R.H. Paediatric Department for a while and also to a children's hospital. Continued to make no progress. Had a severe tetraplegia and E.E.G. showed marked changes of the hypsarrhythmic type. Admitted as an emergency at the age of two years with high fever and possible pneumonia. Died a few hours later. Autopsy showed no sign of pneumonia. Macroscopic examination of the cerebrum: large difference between the right and left side. Large cyst corresponding to the whole of the left temporal lobe. Microscopy: polyporencephaly as a consequence of cerebral anoxia.

Diagnosis: oligophrenia (idiotcy), spastic tetraplegia, infantile spasms and hypsarrhythmia.

Summary: a boy whose mother vomited during pregnancy. The child was restless from the age of a month and from the age of 4 months had infantile spasms. E.E.G. showed changes of hypsarrhythmic type. V.E.G. at 6 months showed a ratio of 0.39,

3rd ventricle 11 mm. His condition deteriorated and he developed a severe tetraplegia. Died in high fever at the age of two years.

218.

N.K. no. 23456/55. Boy born 29.12.48. No familial predisposition. Only child. Pregnancy: nausea and vomiting from the third month. Pneumonia in the 7th month. Albuminuria and hypertension. Had eclampsia and was treated medically. Delivery: asphyxia. Given injections. Birth weight 3200 g.

Symptoms: harelip. No convulsions at birth. Operation for harelip at 3 months and at about that time the parents noticed that there was apparent brain damage. At 7 months he had a convulsion. Sat alone at a year and walked alone at 3 years. Had convulsions at long intervals. Examined in a children's hospital at the age of 2 years 2 months. I.Q. low and almost unmeasurable. Admitted to R.H. Paediatric Department at the age of 6 years. Right-sided hemiplegia. Severely abnormal E.E.G. X-ray of skull showed no definite abnormality. Then treated as an out-patient in the R.H. Paediatric Department. Physical examination at the age of 6½ showed him to be almost paraplegic.

Admitted to N.K. department a month later.

S.E.G: pressure 250, clear fluid. Ratio 0.39 (0.30/0.48). 3rd ventricle 11 mm. No complications after the investigation.

Left-sided arteriography: no definite abnormality.

Follow-up: had been under State mental care for many years and continued to attend the R.H. Paediatric Department as an out-patient. Seizures have increased lately. E.E.G. unchanged. Tendon reflexes generally brisk. Diagnosis: tetraplegia with right-sided predominance. Vocabulary has improved and he has become toilet trained. Does well at a special kindergarten.

Diagnosis: oligophrenia (imbecility), spastic tetraplegia (right side more involved than left), epilepsy.

Summary: a boy whose mother had a complicated pregnancy. He was asphyxiated at birth and had a harelip. Convulsions developed at 7 months and development was slow. S.E.G. at 6½ years showed a ratio of 0.39, 3rd ventricle 11 mm. Is in a special kindergarten, continues to have seizures and has a predominantly right-sided tetraplegia.

219.

N.K. no. 21774a/54. Girl born 16.5.47. No familial predisposition. Only child. Pregnancy normal. Delivery by breech presentation and fairly severe asphyxia present. Birth weight 3300 g.

Symptoms: flaccidity of left arm noticed on third day of life. Had a haematoma on the right side of the neck. Admitted to hospital at 3 months. Lumbar puncture showed bloodstained fluid at first followed by yellow fluid. Development was retarded.

First admission to N.K. department at the age of 16 months. Eyes: slight convergent squint. Could not raise herself, sit, stand or walk. Head circumference 48 cm. Left-sided hemiplegia present. Bilateral sub-dural puncture showed clear fluid.

S.E.G: pressure 250. Pictures showed pronounced dilatation. Ratio judged to be about 0.40 (0.50/0.35). 3rd ventricle?

Follow-up: examined and treated as an out-patient in the R.H. Paediatric Department. E.E.G: extreme side difference with no activity on the right side. Eyes: convergent squint still present. Second admission to N.K. department when nearly 7 years old. Head circumference 56 cm. Appeared alert and normally developed. Reflexes continued to be increased on the left side. Right-sided arteriography performed. This showed the anterior cerebral artery to be severely dilated. No support for sub-dural hygroma. No complaints after examination. Continues to be followed up in the R.H. Paediatric Department and is making steady progress. Has some difficulty in using left arm and there is a left-sided spastic hemiplegia. Speech is good. Head circumference 57.2 cm. No seizures. Intelligence difficult to assess but presumably reduced.

Diagnosis: left-sided spastic hemiplegia, ? intellectual inferiority.

Summary: a girl who was asphyxiated at birth and had a flaccid paresis of the left

arm. Sequelae of intracranial haemorrhage noticed at 3 months and S.E.G. at 4 months showed a ratio of 0.40. E.E.G. was abnormal but right-sided arteriography excluded a sub-dural hygroma. There is a left-sided spastic hemiplegia and reduced intelligence.

220.

N.K. no. 05656/50. Boy born 24. 10. 49. No familial predisposition. Second of two children. Pregnancy normal. Delivery medically induced, otherwise normal. Birth weight 3750 g.

Symptoms: vomiting since the age of 5 months accompanied by flaccidity and weight loss. Admitted to the R.H. Paediatric Department at the age of 6 months. Had a short episode of cyanosis, jerks in the face and becoming withdrawn. Sub-dural puncture on the left side normal. On the right side there was artificial bleeding. X-ray of skull normal.

Admitted to N.K. department at the age of 17 months. Eyes normal. Head circumference 44 cm. Muscles around the mouth appeared somewhat atrophic. Was dull and sleepy. Reflexes normal. Sub-dural puncture revealed clear fluid on both sides.

V.E.G: pressure 0. Ratio 0.40 (0.45/0.35). 3rd ventricle 7 mm. In the anterior part of the right hemisphere the picture resembled porencephaly. No temperature or other complication following the examination.

Follow-up: the family doctor reported that patient died at home at the age of 8 months. The brain condition was complicated by anaemia. Cause of death: heart stop.

Diagnosis: encephalopathy, possible epilepsy.

Summary: a boy who at 5 months had vomiting, flaccidity and loss of weight. Possible seizures occurred at 6 months. V.E.G. at that time showed a ratio of 0.40, 3rd ventricle 7 mm. Died at home at 8 months.

221.

N.K. no. 07133/51. Boy born 25. 10. 50. No familial predisposition. Only child. Pregnancy normal apart from hormone injections during the first month. Delivery 3 weeks premature. Birth weight 2750 g.

Symptoms: head rotated to the left from birth. Deviation of gaze and nystagmus to the left noticed at 2-3 months. Admitted to a paediatric department where left-sided fontanelle puncture showed yellow fluid and increased albumin content.

Admitted to N.K. department at the age of 5 months. Head circumference 43 cm. Head turned towards the left. Slight convergent squint and undulating nystagmus. Appeared retarded physically. Reflexes normal. X-ray of skull showed some flattening in the left temporal region.

S.E.G: pressure 400, clear fluid. Ratio 0.40 (0.35/0.45). 3rd ventricle 9 mm. Normal surface air. No complications after the examination.

Follow-up: admitted to a paediatric department at the age of 21 months. Diminished function of right-sided extremities found with 3 cm. shortening of right leg. Child lay in opisthotonus position. Admitted to a nursery home under State mental care at the age of 3 years 8 months. At first appeared severely oligophrenic but improved somewhat. Was rather aggressive towards other children. No convulsions. Right arm held slightly paralysed with hand in claw position. Physical examination: normal, healthy appearance. Head circumference 52.5 cm. Right-sided convergent squint but no nystagmus. He has a severe right-sided hemiplegia with malposition of the hand and shortening of the leg, also subluxation of the right hip. Patellar reflexes on the right with area extended over whole tibia. Right-sided Babinski. Can walk with support and sits up well. Hearing is normal and he answers to his name.

Diagnosis: oligophrenia (imbecility), right-sided spastic hemiplegia.

Summary: a boy whose head was turned to the left from birth and who also had eye signs. At the age of 5 months S.E.G. showed a ratio of 0.40, 3rd ventricle 9 mm. He is in a State mental institution, is severely mentally retarded and has a right-sided hemiplegia.

222.

N.K. no. 23474/55. Girl born 13. 10. 54. Familial predisposition: cousin admitted to hospital for epileptics because of brain atrophy. Fifth of five children. Pregnancy:

the mother was knocked down by a scooter during the fourth month without apparent ill-effect, in particular there was no haemorrhage. Delivery full-term and rather fast. Stimulant injections given. Birth weight 2800 g.

Symptoms: cried very weakly. No neonatal jaundice. Convulsions occurred at 4-6 months of age with jerks in the arms. No loss of consciousness. At the age of 6 months it was noticed that motor development was retarded. She did not seem to recognise her parents and at about that time the convulsions increased up to 10-20 a day, lasting a few seconds. No loss of consciousness and the child seemed alert and in good condition after the convulsion.

Admitted to N.K. department at the age of 8 months. Eyes: alternating convergent squint. Co-operated well during the examination. Head circumference 42 cm. Muscle tone moderately increased in the legs and severely increased in the arms. Hands held clenched in spastic position and there was ankle clonus, inconstant Babinski and brisk patellar reflexes. X-ray of skull normal. E.E.G. severely abnormal with depression of activity over right hemisphere and a focus in the right fronto-temporal region.

V.E.G.: pressure 200, clear fluid. Ratio 0.41 (0.38/0.44). 3rd ventricle 9 mm. There was a frontal air collection, more pronounced on the right side. Temperature 38.3° C. the same day, otherwise no complications. Biopsy from right side of cortex showed slight ganglion cell degeneration.

Follow-up: treated and followed up in the Orthopaedic Hospital's cerebral palsy clinic. Diagnosed at the age of 2 years as a case of cerebral palsy, cerebral atrophy, spastic tetraplegia, epilepsy (paroxysmal dysrhythmia), debilitas mentis or imbecility, alternating convergent squint. The family thinks there has been some progress. She can now turn over, enjoys being played with and wants toys. Is seizure-free on phenobarbitone. Can sit if strongly supported. Cannot chew but swallows well. Physical examination: head circumference 46 cm. Otherwise as before.

Diagnosis: spastic tetraplegia (arms more affected than legs), convergent squint, previous epilepsy, oligophrenia (? debilitas, ? imbecility).

Summary: a girl whose mother was involved in a road accident during the 4th month of pregnancy. From the age of 4-6 months she had increasing convulsions. V.E.G. at 8 months showed a ratio of 0.41, 3rd ventricle 9 mm. Cortical biopsy showed slight ganglion cell degeneration. She is mentally retarded and has a spastic tetraplegia. Seizures are controlled by phenobarbitone.

223.

N.K. no. 02267/48. Boy born 20.4.47. Familial predisposition: mother's brother has dementia praecox. Second of two children. No information on pregnancy. Delivery normal. Birth weight 2500 g.

Symptoms: severe retardation, flaccidity and apathy noticed at the age of 6 months. At the age of 12 months he still could not crawl. At the age of 14 months irregularly spaced convulsions occurred as rhythmic twitchings round the left side of the mouth spreading to the cheek and eventually to the left arm and leg. During the months immediately prior to admission the convulsions had apparently involved all four extremities. Convulsions occurred up to four times a day and during these he was withdrawn and did not react when spoken to. Admitted to a paediatric department at the age of 14 months. Subdural puncture on the right side was normal. No fluid obtained from the left side.

Admitted to N.K. department at the age of 16 months. Was flaccid and dull. Could sit but could not stand or walk. Eye examination: could focus. No abnormality found. "Cracked pot" sound on cranial percussion. Head circumference 46 cm. Reflexes normal. X-ray of skull normal. E.E.G. showed no definite abnormality. Frequency of activity possibly too slow.

V.E.G.: pressure 0, clear fluid. Ratio 0.43 (0.40/0.47). 3rd ventricle not measurable. No complications.

Follow-up: patient was admitted to a State mental institution and discharged at the age of 5 years 8 months after a stay lasting 2 years 7 months. He has since been in a home for retarded children and has learnt to walk and to feed himself. Toilet training is improving but is not yet complete. Has no seizures. Physical examination: severely

oligophrenic and it is almost impossible to make any contact with him. He moves almost as though blind with small careful steps. He is tense and stiff and has brisk tendon reflexes with extended patellar reflex areas. Doubtful Babinski and no ankle clonus. Head circumference 50 cm. No squint. Looks at his fingers the whole time and dribbles. Grinds his teeth violently.

Diagnosis: oligophrenia (idiocy), previous epilepsy, motor retardation (? spastic paraplegia).

Summary: a boy who from the age of 6 months was noticed to be mentally and physically retarded and from the age of 14 months had convulsions, primarily left-sided but later generalised. V.E.G. at 16 months showed a ratio of 0.43, 3rd ventricle not measureable. Is in a home for mentally retarded children. Is severely oligophrenic with motor retardation and a possible spastic paraplegia. Has no convulsions.

224.

N.K. no. 06021/50. Boy born 8. 6. 49. No familial predisposition. Only child. Pregnancy normal. Delivery prolonged, for which reason injections given. Asphyxia for 15 minutes. Birth weight 4000 g.

Symptoms: opisthotonus seen at birth. Development retarded and at 8 months uncertainty of movement of the right hand noticed.

Admitted to N.K. department at the age of 14 months. Eyes: could not look to the right. Left-sided divergent squint and right-sided homonymous hemianopia. Head circumference 46 cm. Spastic paresis of right-sided extremities, particularly the arm. Tendon reflexes brisker on the left side. Doubtful right-sided Babinski. Definite left-sided Babinski. X-ray of skull: pronounced dolichocephaly. Slightly deep posterior fossa.

V.E.G.: pressure 80, clear fluid. Ratio 0.43 (0.37/0.49). 3rd ventricle 12 mm. Increased surface air frontally. Following the examination the temperature rose to 39.3° C. and there was neck stiffness. On cisternal puncture pus was found. Because of a suspected abscess V.E.G. was repeated and excluded this. There were, however, no really adequate pictures so a definite measurement was not possible. The ratio for the whole system was 0.49. He was febrile for two days after the examination.

Follow-up: followed up in the R.H. Paediatric Out-patient Department. Developmental quotient at the age of 4 years was 20. No real progress has been made and the child is under State mental care. Neurological examination showed a spastic tetraplegia and E.E.G. was possibly abnormal.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia.

Summary: a boy whose delivery was prolonged and who was asphyxiated for 15 minutes. Opisthotonus noticed at birth together with retarded development. V.E.G. at 14 months showed a ratio of 0.43, 3rd ventricle 12 mm. The examination was followed by fever and neck stiffness. Repeated examination showed a ratio of 0.49. The patient is under State mental care and has a spastic tetraplegia.

225.

N.K. no. 04845/50. Girl born 28. 1. 49. No familial predisposition. Only child. Pregnancy normal. Delivery difficult and forceps were used. There was, however, no asphyxia. Birth weight 3050 g.

Symptoms: would not take the breast. At the age of a year could still not sit alone nor play with a rattle and did not move about as much as other children. Admitted to the R.H. Paediatric Department. X-ray of skull normal. Developmental quotient 56.

Admitted to N.K. department at the age of a year. Appeared oligophrenic. Eyes: alternating convergent squint. Head circumference: 43 cm. Bilateral Babinski and brisk tendon reflexes. Both legs spastic. X-ray of skull normal. Doubtful left-sided facial nerve paresis.

V.E.G.: pressure 120. Ratio 0.45 (0.42/0.49). 3rd ventricle 8 mm. Temperature 38.4° C. the same day, normal on the third day. Was very restless and cried a great deal.

Follow-up: treated as an out-patient in the R.H. Paediatric Department. Is intellectually very retarded and has a pronounced paraplegia and possibly slight changes in the arms.

Head circumference 49.8 cm. Brisk tendon reflexes in both legs, Babinski and ankle clonus. Increased tendon reflexes in the arms.

Diagnosis: oligophrenia (imbecility), spastic tetraplegia (legs more affected than arms).

Summary: a girl who had a difficult forceps delivery. There was mental and physical retardation from birth. V.E.G. at a year showed a ratio of 0.45, 3rd ventricle 8 mm. She is very retarded and has a spastic tetraplegia.

226.

N.K. no. 08552/52. Boy born 19. 6. 51. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3500 g.

Symptoms: jaundiced for 14 days. Cried a lot when 2-3 months old and at 5 months had an episode of cyanosis, vomiting and jerks in all extremities, lasting a few minutes. Similar episodes followed and occurred 3-4 times a day. Admitted to hospital and transferred to the R.H. Paediatric Department. The seizures increased and almost resembled status epilepticus, mainly affecting the left side. Eyes: possible atrophy of the optic nerve. X-ray of skull: prominence corresponding to the occipital bone, otherwise no abnormality. E.E.G. showed severe dysrhythmia.

Admitted to N.K. department at the age of 6 months. Eyes: possible atrophy. Constant nystagmus but could focus. Head circumference 41.5 cm. Head usually turned to the right. Could not swallow. Extended patellar reflex zones. Bilateral Babinski. E.E.G: severe dysrhythmia with bilateral spike foci.

S.E.G: pressure 150, clear fluid. Ratio 0.46 (0.50/0.43). 3rd ventricle 10 mm. Was febrile before the examination and temperature was 38.5° C. the day after the examination. Otherwise no complications.

Follow-up: admitted to a State mental institution for four months at the age of two years. His condition continued to be poor and the generalised convulsions became more frequent and severe. He was not toilet trained and was completely helpless. Physical examination shortly after admission showed him to be a very sick and emaciated child who performed athetoid arm and leg movements. Head circumference 43 cm. Extremities: slightly spastic with inconstant Babinski but no ankle clonus. *Diagnosis:* tetraplegia with athetosis, microcephaly and idiocy. When aged 2 years 8 months he developed pneumonia with high fever and in spite of antibiotics his condition deteriorated and he died. Autopsy: bilateral bronchopneumonia. Brain autopsy: progressive cerebral poliodystrophy consequent to cerebral anoxia.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, epilepsy.

Summary: a boy who had slight jaundice for two weeks and from the age of 5 months increasing seizures. S.E.G. at 6 months showed a ratio of 0.46, 3rd ventricle 10 mm. He was placed in a State mental institution where he continued to have convulsions and was severely retarded. He died at the age of 2 years 8 months from pneumonia.

227.

N.K. no. 09514/52. Girl born 17. 2. 51. No known familial predisposition. Only child. Pregnancy normal. Delivery lasted 72 hours, was by breech presentation and was severe. Forceps were used. There was slight asphyxia. Birth weight 4100 g.

Symptoms: was said to have had intracranial haemorrhage at birth. Convulsions and cerebral cry immediately after and development was slower than usual, especially mental development. Convulsions continued and particularly involved the right-sided extremities. Admitted to the R.H. Paediatric Department at the age of a year. L.E.G. ratio 0.48 (0.43/0.51). 3rd ventricle not measureable. Right side - 10 mm. X-ray of skull showed it to be thin-walled. E.E.G. showed severe dysrhythmia localised to the right temporo-frontal region. Developmental quotient 44.

Admitted to N.K. department at the age of 18 months. Eyes: left-sided convergent squint. Head circumference 43 cm. Could not sit alone. There was malpositioning and increased muscle tone of the right arm and leg. X-ray of skull normal. E.E.G: severe depression of activity over the left hemisphere.

S.E.G: pressure 150, clear fluid. Ratio 0.47 (0.38/0.58). 3rd ventricle 5 mm. Temperature 38° C. the third day, otherwise no complications.

Follow-up: admitted to a State mental institution at the age of 2 years 4 months. Diagnosis: imbecility, petit mal. During her admission she made some progress. Treatment given for her spasticity. Understood all that was said to her but could not talk. Was not toilet trained and had to be helped with everything. Over the years has had very occasional petit mal seizures. Physical examination: looks happy. Easy to make contact with and appears wide awake but does not say anything. Head circumference 46.8 cm. Can walk a few steps alone without too much difficulty. Reflexes: spastic tetraplegia with changes chiefly affecting the legs.

Diagnosis: oligophrenia (imbecility), spastic tetraplegia (legs more affected than arms) epilepsy (petit mal).

Summary: a girl whose birth was by forceps because of a difficult breech presentation. She was asphyxiated and there were immediate signs of intracranial haemorrhage. Development was slow and she had convulsions. L.E.G. at a year showed a ratio 0.48, right side - 10 mm. S.E.G. at 18 months showed a ratio of 0.47, 3rd ventricle 5 mm. Is in a State mental institution and has spastic tetraplegia and rare petit mal seizures.

228.

N.K. no. 05816/50. Boy born 7. 6. 42. No familial predisposition. First of three children. Pregnancy complicated by pyelitis in the third month. Delivery 11 weeks premature, breech presentation. Birth weight 1500 g.

Symptoms: not expected to live. Spent the first four months in a paediatric department because of poor general condition and was always very retarded. Walked at 2 years and began to talk at 3 years. Was periodically very miserable as though he had pain in his head. Admitted to a paediatric department at the age of a year because of otitis media, a stomach disorder and pneumonia. Re-admitted on many further occasions because of various illnesses.

Admitted to N.K. department at the age of 8 years. Appeared very retarded. Head circumference 55 cm. Eyes excessively myopic with bilateral exophthalmos. Speech very stereotyped and motor ability poor. Reflexes normal. X-ray of skull normal. E.E.G. probably normal.

S.E.G: pressure 400, clear fluid. Ratio 0.48 (0.44/0.51). 3rd ventricle did not appear dilated. Temperature 38.4° C., otherwise no complications.

Follow-up: contracted aparalytic poliomyelitis at the age of 10 years. Attended a special school until his admission to a State mental institution at the age of 13 years 3 months. Diagnosis: imbecility. He is remarkably well-developed and well-adjusted. Can talk and answers questions. Hearing is reduced but he understands remarks made to him directly. Is rather clumsy and cannot dress himself correctly. I.Q. at 4 years 41, 9 years 51, 13 years 45 and 42. Physical examination: head circumference 58 cm. Severely myopic. Tendon reflexes generally brisk. Joint movements free and there is no spasticity, ankle or patellar clonus. Is very deaf. Appears pseudo-intelligent. Puberty is beginning.

Diagnosis: oligophrenia (imbecility), deafness.

Summary: a boy whose mother had pyelitis during the third month of pregnancy and whose birth was 11 weeks premature. His neonatal condition was extremely poor and development was slow. S.E.G. at 8 years showed a ratio of 0.48. He is in a State mental institution and though an imbecile appears remarkably well-developed and well-adjusted. Both his hearing and his vision are reduced.

229.

N.K. no. 08282/51. Boy born 9. 10. 47. No familial predisposition. First of two children. Pregnancy: pyelonephritis and hypertension. Delivery prolonged, forceps used. Presumably no asphyxia. Birth weight 4250 g.

Symptoms: rickets at the age of 5 months and subsequent development was retarded. Began to walk at 18 months but had "influenza" and paralysis of the left side of the body. Began to walk again at 3 years and shortly afterwards had another attack of "influenza." Generalised convulsions followed and were accompanied by rigidity. Six months before admission his condition deteriorated after a fall on his head and he was said to be retarded.

Admitted to N.K. department at the age of 4 years. Eyes normal. Sat and lay normally. Played normally. Did not immediately appear mentally deficient. There was moderate paresis of the left arm and pronounced spasticity of both legs. Gait was unsure and broad-based. Tendon reflexes were very brisk. Babinski was doubtful on the right, definite on the left. X-ray of skull: deep posterior fossa. E.E.G. showed dysrhythmia.

S.E.G.: pressure 150, clear fluid. Most of the air was outside.

V.E.G.: two days later. Pressure 90, clear fluid. Ratio 0.52 (0.58/0.46). 3rd ventricle 21 mm. Temperature 37.9° C. No complications.

Follow-up: the Medical Officer in Reykjavik wrote to say that the patient was epileptic and mentally deficient and spent most of his time in an institution.

Diagnosis: oligophrenia (? degree), epilepsy, cerebral palsy.

Summary: a boy whose mother had pyelonephritis during pregnancy and whose delivery was by forceps with possible asphyxia. At the age of 18 months he had a febrile illness with left-sided hemiparesis and again at the age of 3 years. This was followed by generalised convulsions and retarded development. V.E.G. at 4 years showed a ratio of 0.52, 3rd ventricle 21 mm. His condition is very poor; he has epilepsy and is mentally retarded. He spends most of the time in an institution.

230.

N.K. no. 22533/54. Boy born 1. 12. 53. Familial predisposition: a cousin is a mongoloid idiot. Fifth of five children (the first died at the age of a month from a heart disorder and the second was still-born). Pregnancy and delivery normal. Birth weight 3800 g.

Symptoms: at the age of two months had bronchitis and after that spasticity of legs was noticed. He also cried a great deal and rolled his eyes after eating. Admitted to hospital at the age of 3 months because of intestinal disorder. Subluxation of the left hip was found and tonic convulsions observed. Admitted to the R.H. Paediatric Department at the age of 6 months and again at 10 months. Diagnosis: spastic tetraplegia. E.E.G. severely abnormal. X-ray of skull normal. Eyes: unco-ordinated movements.

Admitted to N.K. department at the age of 9 months. Appeared retarded. Eyes: nystagmus. Could not focus, did not grasp objects, could not sit alone or hold his head up. Head circumference 42.5 cm. Pronounced generalised spasticity, particularly in the legs. Babinski and brisk tendon reflexes.

V.E.G.: pressure 120, clear fluid. Cortical atrophy seen through both burr holes, particularly on the right side. Ratio 0.52 (0.47/0.56). 3rd ventricle 13 mm. Increased surface air. Somewhat dull and flaccid during the 24 hours after the examination. Temperature 38.5° C. the day after, normal on the fourth day.

Follow-up: admitted to a State mental institution at the age of 15 months and diagnosed as a case of oligophrenia (idiocy). Head circumference on admission was 42.5 cm. and his face was abnormally broad. There was pronounced spasticity and rigidity with early contractures of the elbows and mains d'accoucheurs. Brisk patellar reflexes and left-sided Babinski. Was very dull and motor development was almost non-existent. He was also possibly deaf, was not toilet-trained and had to be helped with everything. During two days he had four severe seizures and numerous petit mal attacks. Three days after admission he developed a high temperature which continued to rise in spite of antibiotics. He lay in a semi-comatose state and had many myoclonic seizures. He died in hyperpyrexia of 41.5° C. Cause of death: encephalopathy consequent to febrile colds, severe epilepsy, hyperpyrexia. No autopsy.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, epilepsy.

Summary: a boy with family history of mental deficiency. After bronchitis at the age of two months he developed spasticity. Convulsions followed and development was retarded. V.E.G. at 9 months showed a ratio of 0.52, 3rd ventricle 13 mm. Cortical atrophy seen through burr holes. Was placed in a State mental institution and died shortly after admission in hyperpyrexia after a cold.

231.

N.K. no. 23352/55. Boy born 3. 6. 54. No familial predisposition. Pregnancy normal. Delivery difficult by forceps with severe asphyxia lasting 45 minutes. Birth weight 2610 g.

Symptoms: immediately admitted to a paediatric department. Was very poorly for the first month, apathetic and cyanotic. At the age of 5 months he was transferred to a State mental institution. Admitted to the R.H. Paediatric Department at the age of 10 months because of loss of weight and vomiting. X-ray of skull showed plaques of calcification on the parietal bone corresponding to an external cephalic haematoma.

Admitted to N.K. department at the age of 11 months. Eyes: possible atrophy of the optic nerve. Head circumference 39 cm. Marked generalised spasticity. E.E.G.: slow activity with high amplitude and numerous single spikes.

V.E.G.: pressure 110, clear fluid. Ratio 0.76 (0.70/0.81). 3rd ventricle appeared very dilated but was not measureable. Sub-dural air particularly on the right side. Temperature 39.2° C. the same day lasting until discharge. Cortical biopsy showed slight meningeal reaction, otherwise no definite pathological changes.

Follow-up: died in hospital 9 days after discharge from the N.K. department. His condition deteriorated and his temperature continued to rise in spite of antibiotic treatment. Autopsy: brain weight 340 g. Diagnosis: polyporencephaly and internal hydrocephaly (consequent to cerebral anoxia), thrombo-phlebitis of the left Sylvian fissure.

Diagnosis: oligophrenia (idiotcy), spastic tetraplegia.

Summary: a boy who had a difficult forceps delivery and was asphyxiated for 45 minutes. There were severe neonatal symptoms and he was placed in a State mental institution at the age of 5 months. V.E.G. at 11 months showed a ratio of 0.76, 3rd ventricle not measureable. He died shortly after discharge in hyperpyrexia.

232.

N.K. no. 07148a/51. Girl born 10. 4. 49. No familial predisposition. Pregnancy normal. Delivery followed by a brief period of asphyxia. Birth weight 4125 g.

Symptoms: when a little more than a year old she sustained a minor head injury without immediate ill-effects. Three days later, however, she had a brief episode of trembling and flaccidity which recurred a few hours later. She was admitted to hospital where the seizures continued. They were of the tonic-clonic type and usually generalised. Admitted to the R.H. Paediatric Department at the age of 11 months. During the night before transfer to N.K. department there were 28 seizures in spite of intensive treatment.

Admitted to N.K. department at 11 months. Eyes turned to the left. She was completely withdrawn and performed continuous athetoid movements, particularly of the arms.

V.E.G.: pressure 0. Ratio 0.28 (0.25/0.31). 3rd ventricle 5 mm. Left side—5 mm. No complications after the examination. A linear fracture was seen in the left occipital region but no haematoma. The cortex on the left side was hyperaemic and showed stasis. The brain tissue was soft and appeared structureless.

Second admission to N.K. department at the age of two years. Patient was well and had begun to talk. Six weeks before admission she had had a new seizure in connection to slight fever. Admitted to hospital in status epilepticus and transferred to a hospital for epileptics. On admission it was thought that she could not see or hear. Physical examination: eye examination revealed macular degeneration and aimless movements with no reaction to light. Hearing doubtful. Could only walk with strong support. E.E.G. showed dysrhythmia over the left hemisphere.

S.E.G.: pressure 210, clear fluid. Ratio 0.29 (0.25/0.34). 3rd ventricle 5 mm. Left side—9 mm. Increased surface air on the left side. Temperature 38° C. the same day, otherwise no complications. Exploratory burr holes performed on both sides. No sub-dural hygroma found.

Follow-up: the patient has since been admitted four times to a hospital for epileptics. On admission at the age of 5 years she had improved a great deal though was still not toilet-trained. She did not appear mentally retarded and perhaps not even dull. Eyes reacted to light. She was deaf and dumb and had been provided with a hearing-aid but had had to give it up. Since the age of 7 years she has not had any seizures. She is lively and understands more than she did. E.E.G. at 7 years showed moderately severe diffuse dysrhythmia. L.E.G. at 5 years showed a ratio of 0.31 (0.31/0.31). 3rd ventricle 5 mm. It is the parent's impression that over the years there has been slow but continuous progress.

She does not talk but hears to a certain extent though exactly how much it is difficult to say. It is not certain how much she can see but she can definitely see things close to her. Her gaze is, however, very staring. She occupies herself all day by copying her mother as she does her housework. Her parents are sure that with some reservations concerning sensory ability her intelligence is good. She walks and runs normally, can hop and stand on one leg. Head circumference 53 cm. No squint or nystagmus. Neurological examination normal.

Diagnosis: multiple sensory defects (speech, hearing and ? sight), epilepsy (? past), possible intellectual inferiority.

Summary: a girl who was asphyxiated for a short while at birth. She sustained a minor head injury at the age of a year which was followed three days later by trembling and flaccidity. V.E.G. at 11 months showed a ratio of 0.28, 3rd ventricle 5 mm. A fracture was seen in the left occipital region. Because of repeated seizures and possible sensory defects S.E.G. was performed at two years. Ratio 0.29, 3rd ventricle 5 mm. Has spent several periods in an epileptic hospital and made definite progress. Her vision is decreased and her intelligence is presumably not equivalent to her age. She has had no seizures for the past year and motor ability is normal.

233.

N.K. no. 52/34. Boy born 10. 11. 25. No familial predisposition. Pregnancy and delivery normal. Birth weight not known.

Symptoms: at the age of 6 months he hit his head against an iron rim and was unconscious for a few minutes. At the age of 4 years he had two head injuries within a short space of time, first hitting his left temple without loss of consciousness and then falling and hitting the back of his head. Two hours later he became increasingly sleepy, lost consciousness and had right-sided convulsions which lasted 12 hours. Admitted to hospital where he slowly regained consciousness. The right side was paralysed. After this he had convulsions at monthly intervals which began in the right hand and gradually became generalised and were accompanied by loss of consciousness. The duration of the convulsions varied between half an hour and several hours. There was right-sided post-paroxysmal paresis, severe headache and occasional distortion of the face. There was also a brief period of reduced vision in the right eye about a year before admission and an isolated incident of diplopia. For a few months before admission there had been transitory deafness. He had previously been very retarded but had improved just before admission.

Admitted to N.K. department at the age of almost 9 years. Eyes: right-sided divergent squint. Right-sided hemiparesis with astereognosis. Right-sided Babinski. X-ray of skull normal.

V.E.G.: ratio 0.31 (0.28/0.34). 3rd ventricle 3 mm. Left side - 18 mm. Temperature 38° C. the day after, otherwise no complications.

Operation over the left motor region revealed atrophic cortex with small, narrow gyri. Approximately corresponding to the middle of the posterior central gyrus was a scar-like area with several 2×3 mm. plaques of calcification. A small artery through the area was coagulated. No post-operative complications.

Follow-up: operated on in an orthopaedic hospital at the age of 13 years for transplantation of the right gastrocnemius muscle and elongation of the right Achilles tendon. Was admitted to a hospital for epileptics from the age of 17-18 years. *Diagnosis:* traumatic epilepsy (Jacksonian), psycho-infantilism. Has since either been in a hospital for epileptics or under their supervision. Stayed at school until the age of 16 but has not attempted to work. "I might get tired and sick." L.E.G. at 17 showed a small amount of surface air. Right ventricle appeared normal, left ventricle dilated. During admission at the age of 21 he was transferred to a home for chronic epileptics for training. He made progress during the first year but convulsions and petit mal then increased and he had to be re-admitted to the epileptic hospital L.E.G. ratio 0.28/0.33. 3rd ventricle 4 mm. Left side - 16 mm. Left-sided arteriography: slight displacement downwards of the media group, otherwise no abnormality. He was transferred back to

the home for epileptics at the age of 28 where he has remained since. His condition is unchanged. He is very sensitive and quite unable to lead an independent existence.

Diagnosis: right-sided spastic hemiplegia, Jacksonian epilepsy, intellectual inferiority.

Summary: a boy who during childhood had several minor head injuries. After one at 4 years he lost consciousness and had increasing right-sided convulsions. V.E.G. when almost 9 years showed a ratio of 0.31, 3rd ventricle 3 mm. Left side - 18 mm. At operation over the left motor region scar formation in the posterior central gyrus was seen with calcification. He is in a home for chronic epileptics, continues to have seizures, has a right-sided spastic hemiplegia and cannot lead an independent life.

234.

N.K. no. 1556/39. Girl born 1.3.30. No known familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight unknown.

Symptoms: admitted to hospital at the age of a year because of a head injury accompanied by right-sided convulsions. Craniotomy performed and no epidural or subdural haemorrhage found. After this she had some uncertainty of the right arm and leg. Over a number of years there were nightly convulsions and loss of consciousness.

Admitted to N.K. department at the age of 9 years 3 months. Left-handed. Scar of craniotomy. Eyes normal. Slight right-sided spastic hemiplegia with reduced stereognostic sense on the right side. X-ray of skull normal.

V.E.G.: ratio not measurable on the right side. Left side 0.35 and by using other measurements a ratio was calculated for the entire system: 0.31 (0.29/0.35). 3rd ventricle 3 mm. Cranial wall on the left side appeared rather thick. Left side - 14 mm. Temperature 38.6° C. on the same day and the following two days, otherwise no complications.

Follow-up: the patient has not been examined personally as there had been no answer to repeated questionnaires. There are, however, very detailed reports from various sources, i.e. State mental authorities and invalid pension board. The patient managed fairly well after discharge but could not attend an ordinary school. She was placed under State mental care at the age of 12 years. I.Q. 62. She was married at 22 after sterilisation had been performed. The marriage is happy but the patient cannot do the housework. During a physical examination at the age of 24 slight right-sided spasticity was found. Convulsions continue but are fairly well controlled by anti-epileptic drugs and there may be days to months between them. I.Q. at 21 was 65. She is rather dependent and hysterical.

Diagnosis: oligophrenia (debilitas mentis), right-sided spastic hemiplegia, epilepsy.

Summary: a girl who developed right-sided spastic hemiplegia and convulsions after a head injury at the age of one year. V.E.G. at 9 years showed a ratio of 0.31, 3rd ventricle 3 mm., left side - 14 mm. She is doing fairly well and is married. I.Q. is 65. There is still a right-sided spastic hemiplegia and convulsions which are adequately controlled.

235.

N.K. no. 23412/55. Boy born 4.9.51. No familial predisposition. Second of two children. Pregnancy: albuminuria during the latter part of pregnancy. Delivery 4 weeks premature. No asphyxia. Birth weight 1900 g.

Symptoms: convulsions began in the first 24 hours and lasted until the tenth day. He then seemed to do well until about 10 months when convulsions reappeared and increased. Motor development was rather retarded. On admission to the R.H. Paediatric Department at the age of 3 years 9 months he did not talk. L.E.G. at a year showed a ratio of 0.35 (0.38/0.32). 3rd ventricle 6 mm. Developmental quotient 70. E.E.G.: severe diffuse dysrhythmia. This was unchanged until it became normal at 4 years. He was placed under State mental care at that time.

Admitted to N.K. department at 3 years 9 months.

V.E.G.: pressure 0, bloodstained fluid. During the examination the patient became ill and cyanotic and it was stopped.

S.E.G. 5 days later: pressure 300, clear fluid. Ratio 0.31 (0.36/0.27). 3rd ventricle 5 mm. Right side - 6 mm. Normal surface air. Biopsy showed normal cortex on the left side and slight chronic ganglion cell degeneration on the right.

Follow-up: has since had only one grand mal seizure but continues to have petit mal. Says single words and enjoys playing. Is not toilet-trained. Is under State mental care at home. Physical examination: head circumference 46.5 cm. Physically healthy. Eyes normal. Reflexes brisk but probably not pathological.

Diagnosis: oligophrenia (imbecility), epilepsy.

Summary: a boy whose mother had albuminuria during pregnancy and whose birth was premature. Convulsions occurred during the first ten days of life and reappeared at 10 months. Development was retarded. V.E.G. at 3 years 9 months showed a ratio of 0.35, 3rd ventricle 6 mm. Cortical biopsy showed slight chronic ganglion cell degeneration on the right. Is at home under State mental care. Continues to have petit mal seizures.

236.

N.K. no. 9872/47. Girl born 14. 4. 41. No familial predisposition. Second of two children. Pregnancy normal. Delivery difficult, brow presentation. Asphyxia for 15 minutes. Birth weight 3500 g.

Symptoms: severe jaundice at birth. Difficulty in co-ordinating movements from the age of 6 months, particularly hand movements. She could crawl at the age of 18 months but could not walk without support. Admitted to the R.H. Paediatric Department at the age of 4 years. Eyes normal.

Admitted to N.K. department at the age of 6 years. Eyes normal. Dysdiadochokinesis present. Bilateral Babinski. X-ray of skull: increased digital markings.

S.E.G.: pressure 220, clear fluid. Ratio 0.32 (0.28/0.36). 3rd ventricle 3 mm. Left side - 5 mm. Temperature 39.2° C. the second day, normal on the fourth day. No other complications.

Follow-up: learnt to walk at 10 years. Examined at the Orthopaedic Hospital's cerebral palsy clinic at the age of 13. Diagnosed as a case of cerebral palsy, athetoid tetraplegia, ? intellectual inferiority and dysarthria. She lives in a residential school for physically handicapped. I.Q. could not be assessed but was possibly normal. The test was repeated later and assessed at 67. Is having speech therapy and can use a typewriter. The staff are sure that her I.Q. is at least 80. Gait is steadier and she seldom falls.

Diagnosis: athetosis, intellectual inferiority.

Summary: a girl who was asphyxiated for 15 minutes at birth and had severe jaundice. Co-ordination of movements difficult at 6 months and development retarded. S.E.G. at 6 years showed a ratio of 0.32, 3rd ventricle 3 mm. Left side - 5 mm. She is in a residential school and has a fairly severe athetosis but only slight intellectual deficiency.

237.

N.K. no. 3293/42. Girl born 13. 1. 34. No familial predisposition. Third of four children. Pregnancy and delivery normal. Birth weight 4500 g.

Symptoms: at the age of 7 years the patient fell and hit her head. She was sleepy on the fourth day and six weeks later suddenly lost consciousness. Admitted to hospital and transferred to the R.H. Paediatric Department. I.Q. assessed at 68. Discharged to a convalescent home and from there to a State mental institution. At the age of 8 years had generalised convulsions as well as right-sided convulsions and in the three months prior to admission had petit mal and hallucinations. The latter, however, were not present on admission. There was increasing restlessness and mental reduction and a lack of co-operation.

Admitted to N.K. department at the age of 8 years 4 months. Eyes and neurological examination normal. X-ray of skull: possibly a fracture through the anterior cranial fossa. The patient did not immediately appear mentally retarded but suffering more from character changes.

V.E.G.: pressure 225. Ratio 0.33 (0.30/0.36). 3rd ventricle 3 mm. Left side - 6 mm. Temperature 38.8° C. the day after examination, normal by the third day.

Follow-up: the patient was in a State mental institution from the age of 8 until she returned home at the age of 14. She was withdrawn from State mental care at the age of 20 for economic reasons. I.Q. had been assessed on many occasions and at 7 years was 68, 13 years 43, 17 years 44. At the beginning the patient was very restless

though she could dress herself. Convulsions occurred three times a night and there were many petit mal attacks. At the age of 9 years she was described as considerably restless and crying and having 2-3 convulsions a month. At 13 there was said to be some improvement and her speech was better. She was toilet-trained and could help to look after the other children. Improvement continued over the following years and convulsions decreased in number. At the age of 15 she could look after herself entirely and was completely toilet-trained. When visited at home the patient was said to have had no benefit from education and had not learnt to read or write. She helped at home and could knit and there appeared to have been general improvement at the time of puberty at 13-14 years. Motor ability, sight and hearing normal. Could look after herself and had no convulsions at home. Continues to take anti-epileptic drugs. Physical examination: appeared younger than her age but physically well-developed. Answered sensibly when questioned but not corresponding to her age. Head circumference 54.5 cm. Eyes, reflexes and speech normal.

Diagnosis: epilepsy (? past), oligophrenia (? debilitas mentis).

Summary: a girl who at the age of 7 years had a possible skull fracture followed some time later by convulsions and retarded development. V.E.G. at 8 years showed a ratio of 0.33, 3rd ventricle 3 mm., left side - 6 mm. Spent 5 years in a State mental institution where she continued to have seizures though she improved during the latter part of her stay. She is now at home where she helps a little and manages to look after herself. She has had no seizures over the past few years.

238.

N.K. no. 7534/46. Boy born 23.1.35. No familial predisposition. Pregnancy normal. Delivery 5 weeks premature. Birth weight 2250 g. Second of two children.

Symptoms: development always retarded. He had encephalitis at the age of a year and was admitted to a paediatric department. There was marked right-sided paralysis for some months. Otitis on two occasions at the age of two years. From the age of 3-4 years there was increasing petit mal followed by Jacksonian seizures in the right arm and leg.

Admitted to N.K. department at the age of 11 years. Appeared rather childish. Eyes normal. Had a slight right-sided spastic hemiparesis and was left-handed. X-ray of skull normal. E.E.G. not done.

S.E.G.: pressure 120, clear fluid. Ratio 0.33 (0.26/0.41). 3rd ventricle 10 mm. Left side - 12 mm. Temperature 38.4° C. the same day and also the next day. Normal on the 3rd day.

Follow-up: admitted to a hospital for epileptics at the age of 12 years and to another neurosurgical department at the age of 14. V.E.G. ratio 0.20/0.41. 3rd ventricle 8 mm. Left side - 8 mm. Normal surface air. Admitted to a hospital for epileptics at the age of 15 and has been in a home for chronic epileptics since the age of 20. E.E.G. shows some dysrhythmia evenly distributed. I.Q. at 15 was 59. Physical examination: normal appearance. Slight right-sided spastic hemiplegia. Seizures continue but are less frequent. Head circumference 55.5 cm. Eyes normal.

Diagnosis: epilepsy, right-sided spastic hemiplegia, oligophrenia (debilitas mentis).

Summary: a boy whose birth was 5 weeks premature and who was always retarded. After encephalitis at the age of a year he had a right-sided paresis followed two years later by convulsions. S.E.G. at 11 years showed a ratio of 0.33, 3rd ventricle 10 mm., left side - 12 mm. V.E.G. a few years later showed almost no change. Is in a home for chronic epileptics. Still has a right-sided spastic hemiplegia but seizures are infrequent. Has an I.Q. of 59.

239.

N.K. no. 04402/49. Boy born 5.1.49. No familial predisposition. Third of four children. Pregnancy and delivery normal. Birth weight 3650 g.

Symptoms: jaundiced at birth. Admitted to hospital at two days because of jaundice and crying. There were frequent jerks in both arms but no real convulsions. Could not suck. At the age of a month reduced power of the right arm and leg was noticed.

Admitted to N.K. department at the age of 10 months. Head circumference 43 cm. Eyes normal. Mental development corresponded to his age. Right arm and leg were rigid and the musculature was hypotrophic on the right side. X-ray of skull showed it to be medium-sized, thin-walled with deep posterior fossa.

S.E.G.: pressure 350. Ratio 0.33 (0.27/0.35). 3rd ventricle 8 mm. No air over the left hemisphere, increased air on the right side. Left side - 6 mm. Through a burr hole entry was made into a large intra-cerebral cyst about 2 mm. beneath the cortex. The cyst was filled with clear fluid. Microscopy: chronic arachnoiditis. Temperature the day after was 38.5° C. Normal on the fourth day.

Follow-up: attended a kindergarten for spastic children from the age of 3-7 years. The developmental quotient fell from 76 to 55. Admitted to the R.H. Paediatric Department at the age of 5 and operated on for congenital heart disease (patent ductus arteriosus). Admitted to a paediatric hospital also at the age of 5. L.E.G. ratio 0.30/0.37. Left side - 21 mm. 3rd ventricle 11 mm. At the time of the follow-up examination the patient was rather dull but he could dress and feed himself. Had petit mal seizures but probably no grand mal. Physical examination: head circumference 50 cm. Eyes normal. There is a right-sided spastic hemiplegia with slight changes on the left side. The arm is more affected than the leg. Speech is fairly good and he understands much of what is said to him.

Diagnosis: right-sided spastic hemiplegia (tetraplegia, right side more affected than the left), operation for congenital heart disease, oligophrenia (debilitas mentis).

Summary: a boy who was jaundiced at birth and had muscular spasms neonatally. Decreased function of right arm and leg noticed at one month. S.E.G. at 10 months showed a ratio of 0.33, 3rd ventricle 8 mm, left side - 6 mm. Burr hole on the left side showed a large intra-cerebral cyst about 2 mm. beneath the cortex. Operated on for patent ductus arteriosus. Has a spastic tetraplegia, the right side more affected than the left. Is mentally retarded with an I.Q. of 55. Has occasional petit mal seizures.

240.

N.K. no. 08801a/52. Boy born 10. 1. 49. No familial predisposition. First of two children. Pregnancy normal. Delivery lasted 6-8 hours. There were pressure marks on the head. No asphyxia. Birth weight 3100 g.

Symptoms: at the age of 6 months it was noticed that he could not use his left arm when he crawled and the hand was held clenched. At the age of a year he was seen to drag his left leg. Development was otherwise normal.

First admission to N.K. department at the age of 22 months. Left-sided hemiparesis present with Babinski. Head circumference 47 cm. X-ray of skull normal. E.E.G.: no definite abnormality.

S.E.G.: pressure 300, clear fluid. Ratio 0.33 (0.40/0.27). 3rd ventricle 6 mm. Right side - 8 mm. No surface air. Temperature 38.5° C. the day after, normal on the third day. Otherwise no complications.

He was admitted to a children's hospital at the age of 2 years 7 months and treated by physiotherapy with good but short-lasting effect.

Second admission to the N.K. department at the age of 3 years 2 months because of increasing gait difficulties. E.E.G. normal. Eye examination normal. Head circumference 49.5 cm. Tendency to equinus deformity of the left foot and Babinski.

S.E.G.: pressure 170, clear fluid. Ratio 0.34 (0.42/0.27). 3rd ventricle ? Right side - 10 mm. Temperature 37.9° C. the day after the investigation, otherwise no complications.

Follow-up: the patient has since been followed up in the Orthopaedic Hospital's cerebral palsy clinic. Manages well with leg irons and rides a two-wheeled bicycle. He began to talk rather late. The father feels that he is making steady progress but the mother thinks that progress was most marked at about the age of 3 years. He is well-behaved and sociable and takes care not to expose himself to any danger. Physical examination: normal, healthy appearance. Mental development normal. Head circumference 52 cm. Left-sided spastic hemiplegia not very pronounced. Brisk tendon reflexes in the left arm. Left hand held clenched and not used very much. Hip abduction on the left side to 60° and on the

right to 80°. Left foot can be brought to a right-angle. Babinski present on the left. No definite ankle clonus.

Diagnosis: left-sided spastic hemiplegia, slight dysarthria.

Summary: a boy whose delivery may have been difficult. From the age of 6 months it was noticed that he had a left-sided spastic hemiplegia. S.E.G. at 22 months showed a ratio of 0.33, 3rd ventricle 6 mm. Right side - 8 mm. Because of increasing gait difficulties S.E.G. was repeated at 3 years 2 months. Ratio 0.34, 3rd ventricle 7, right side - 10 mm. He is doing well, has slight dysarthria and a left-sided hemiplegia.

241.

N.K. no. 24977c/56. Boy born 17.11.49. Familial predisposition: father has epilepsy (? post-traumatic) and is a psychopath. Second of two children. Pregnancy normal. Delivery said to be 3 weeks premature and difficult. No asphyxia. Birth weight 4200 g.

Symptoms: at the age of 10 months he had high fever with loss of consciousness and paresis of the right arm. Admitted to hospital where lumbar puncture was found to be normal and paresis disappeared within 24 hours. After discharge he was seen to be holding his right thumb bent into the palm of his hand. Difficulty in using the right foot gradually became apparent and the right arm was used less than the left. Petit mal was also observed and three months before his first admission he had generalised convulsions in connection with tonsillitis. Admitted to the R.H. Paediatric Department. Could stand but not walk. Was not toilet-trained and said only single words. E.E.G. showed severe dysrhythmia. L.E.G. no satisfactory pictures. Ventricular filling incomplete but right side more dilated than left. Increased cortical air on both sides.

Admitted to N.K. department at the age of 20 months. Eyes normal. Head circumference 48 cm. Right-sided spastic hemiplegia present. E.E.G. severe dysrhythmia with spike focus in the left temporo-central region.

S.E.G.: pressure 200, clear fluid. Ratio 0.33 (0.25/0.43). 3rd ventricle 6 mm. Left side - 16 mm. No surface air. No temperature or other complications after the examination.

Re-admitted to the N.K. department at the age of 23 months. Had begun to walk. Petit mal seizures had decreased and no further investigations were carried out apart from E.E.G. which was unchanged.

Follow-up: followed up in the R.H. Paediatric Out-patient department. Hemiplegia had continued. He had become increasingly difficult and aggressive towards his family. Seizures continued in spite of treatment. Re-admitted to the N.K. department at the age of 6 years with a view to hemispherectomy. S.E.G. ratio 0.29 (0.20/0.42). 3rd ventricle 8 mm. Left side - 26 mm. Surface air most pronounced on the left side. Patient was again admitted later that year. E.E.G. continued to be abnormal.

Diagnosis: right-sided spastic hemiplegia, epilepsy, behaviour problems.

Summary: a boy with a family history of epilepsy and psychopathy. Delivery said to have been difficult. At 10 months of age he had high fever and a subsequent right-sided spastic hemiplegia. Petit mal developed followed by generalised convulsions. S.E.G. at 20 months showed a ratio of 0.33, 3rd ventricle 6 mm. Left side - 16 mm. Because of increasing behaviour problems and aggression S.E.G. was repeated at 6½. Ratio 0.29, 3rd ventricle 8 mm. Left side - 26 mm. Hemispherectomy was considered but not performed.

242.

N.K. no. 09799/52. Girl born 30.4.50. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight 3300 g.

Symptoms: severe bronchitis at the age of 2-3 months when she was very ill with a high fever. Following a rise in temperature to over 40° C. she became unconscious, developed paresis of the right side of the body and was admitted to hospital and given antibiotics. Paresis almost disappeared within a week. Admitted to the R.H. Paediatric Department because of a lung disorder at the age of 11 months. Residual hemiparesis still present. There was also an episode when the heart beat very rapidly and vigorously, she dribbled and became rigid but had no real convulsion. Again admitted to the R.H.

Paediatric Department. E.E.G. showed numerous spikes localised to the left occipital region.

L.E.G.: ratio 0.33 (0.28/0.38). 3rd ventricle 7 mm. Left side - 5 mm. No cortical atrophy. Systolic heart murmur heard.

Admitted to N.K. department at the age of 2½ years. Eyes and neurological examination normal. Head circumference 49 cm. Right-sided spastic hemiplegia present. X-ray of skull normal. E.E.G.: spike focus in the left temporo-occipital region.

Left-sided arteriography: no filling of the media cerebral artery.

Right-sided arteriography: no abnormality. No fever or other complication after the examination.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department over a length of time. Seizures have continued in spite of medicine. Developmental quotient at the age of 4 years was above 60. E.E.G. repeated many times showed severe diffuse dysrhythmia. Followed up in a neurological department since the age of 4 years. Is almost seizure-free. Goes to a kindergarten and enjoys it. Heart murmur continues and physiotherapy not given for this reason. No real heart symptoms but she occasionally becomes blue round the lips. Motor ability full and she has developed well particularly since her stay in a convalescent home at the age of 5 years. Now talks very well. The parents think her mental development is two years behind her real age. She is very good at all practical things. Physical examination: head circumference 50 cm. Moderately severe right-sided spastic hemiplegia. The hand, however, is surprisingly capable. No eye symptoms. Mentally she appears to be less retarded than would appear from the parents' evaluation.

Diagnosis: right-sided spastic hemiplegia, epilepsy, intellectual inferiority, congenital heart disorder.

Summary: a girl who after high fever at the age of 3 months developed right-sided paresis for a week. After a lung disorder at the age of 11 months she had a permanent right-sided hemiplegia. There were also uncharacteristic seizures but no real convulsions. *L.E.G.* at 17 months showed a ratio of 0.33, 3rd ventricle 7 mm. Left side - 5 mm. A congenital heart disorder was found. She is doing fairly well, is somewhat retarded intellectually and continues to have a right-sided hemiplegia and occasional epileptic seizures.

243.

N.K. no. 04775/49. Girl born 8. 8. 47. No familial predisposition. Third of three children. Pregnancy: no information. Delivery normal. Birth weight 3300 g.

Symptoms: 2½ months before admission she suddenly refused to eat solid food, was increasingly tired and several days later vomited. Became cyanotic, flaccid, sleepy, crying and irritable. Had several days' fever with cough and sneezing, was very miserable and had black rings round her eyes. Admitted to a paediatric department where no definite abnormality was found.

Admitted to N.K. department at the age of 2 years 4 months. Eyes normal. Rather dull quiet child who only answered yes or no. Stood and walked normally. Reflexes very brisk with extended reflex zones and bilateral Babinski.

V.E.G.: pressure 80, ratio 0.34 (0.31/0.37). 3rd ventricle 8 mm. Right side - 5 mm. Temperature 39° C. the day after the examination, otherwise no abnormality.

Follow-up: attends a normal school and is doing well. Both motor and mental development have been entirely normal.

Diagnosis: healthy.

Summary: a girl who at about the age of 2 years 2 months had fever and vomiting followed by increasing sleepiness and cyanosis. *V.E.G.* at 2 years 4 months showed a ratio of 0.34, 3rd ventricle 8 mm. Right side - 5 mm. She has developed entirely normally.

244.

N.K. no. 05498/50. Girl born 1. 1. 49. No familial predisposition. Only child. Pregnancy uncomplicated. Delivery prolonged and full-term. Membrane rupture was performed. Child was asphyxiated for 30 minutes. Birth weight 2500 g.

Symptoms: jerks down the right side of the body during the first 5 days of life. Walked at 10 months and talked at a year. Right-sided convulsions at the age of 12 and 15 months.

Admitted to N.K. department at the age of 15 months. Alert and lively child. Head circumference 46 cm. Eyes normal. X-ray of skull normal. E.E.G: no definite abnormality but some low frequency activity frontally over the left hemisphere.

S.E.G: pressure 250. Ratio 0.34 (0.31/0.38). 3rd ventricle 6 mm. Left side - 6 mm. No surface air. Temperature 38.3° C. the day after the examination.

Follow-up: admitted to a paediatric department because of seizures at the age of 4-5 years. Was then seizure-free until 7 when minor seizures returned. At follow-up she was still on anti-epileptic treatment. Is in a class corresponding to her age and works hard. No physical disabilities. Physical examination: looks intelligent. Mental development corresponds to age. Head circumference 50 cm. Convergent squint present. Tendon reflexes generally brisk. Bilateral ankle clonus but no Babinski.

Diagnosis: epilepsy.

Summary: a girl who was asphyxiated for 30 minutes at birth and had right-sided convulsions during the first few days of life. S.E.G. at 15 months showed a ratio of 0.34, 3rd ventricle 6 mm. Left side - 6 mm. Was seizure-free from 5-7 years but minor seizures recurred and she continues to take anti-epileptic drugs. Attends a normal school and is healthy.

245.

N.K. no. 06877a/51. Boy born 15. 11. 48. No familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight 3200 g.

Symptoms: when 10 months old the patient fell off a table and hit the left side of his head. He was unconscious for several hours and on admission to hospital was found to have a depressed fracture in the left motor region and a right-sided hemiparesis. Bone fragments were removed at operation and on discharge the paresis had almost disappeared. Six weeks before admission to the N.K. department he had generalised convulsions and momentary loss of consciousness. The convulsions occurred from 1-10 times a day.

First admission to N.K. department at the age of 20 months. Healthy appearance. Eyes normal. Slight irregularity of cranial bone on left side. Doubtful slight left-sided hemiparesis particularly noticeable when walking. Reflexes: no definite abnormality. X-ray of skull: small defect over the left parietal region. E.E.G: severe dysrhythmia.

S.E.G: pressure 550, clear fluid. Ratio 0.34 (0.29/0.41). 3rd ventricle 7 mm. Left side - 10 mm. Temperature 38.5° C. two days later, otherwise no complications.

Operation performed: the dura was adherent over the defect. The cortex was adherent over a 3×2 cm. area where there were clear scar changes. Dura here was removed. Microscopy: dura with sub-dural membrane and bleeding.

Second admission to the N.K. department at the age of 2 years 3 months. His condition had almost become worse since operation. Threatened convulsions with collapse almost every hour when he repeatedly fell and hit the left side of his face. He could hardly walk and did not use his right hand. Examination showed possible optic nerve atrophy on the right side. There was a well-healed operation scar and there seemed to be a right-sided hemiparesis. He could not stand but fell to the left. Doubtful right-sided Babinski. Generalised convulsions were seen during admission. X-ray of skull: sequelae of craniotomy only. E.E.G: severe dysrhythmia.

Operation performed. Incision made through the old scar. The dura was in the process of repair and looked normal. There was marked glial scarring around the two major vessels from the media cerebral artery to the Sylvian fissure. The tissue was markedly degenerated and closely resembled an organised haematoma. The adjacent tissue which was removed was yellow in colour and altered. Post-operative condition was satisfactory.

Follow-up: the patient has had only one convulsion since the age of 3 years and takes no anti-epileptic drugs. He has started school and though a little slow to understand seems to be doing well. The right-sided disability continues, the arm having been operated on at the Orthopaedic Hospital at the age of 7 years. He manages all everyday

requirements himself. He has some difficulty with speech and tends to change words round. Sight and hearing normal. Physical examination: severe spasticity with numerous operation scars. Only slight function of the wrist and cannot stretch fingers, neither can he completely extend the elbow. Right-sided equinus deformity present. Patellar reflexes elicited from the upper third of the tibia. Babinski but no ankle clonus. No Babinski on the left side but rather brisk patellar reflexes.

Diagnosis: right-sided spastic hemiplegia (slight changes on the left side), epilepsy, possible intellectual inferiority.

Summary: a boy who sustained a head injury at the age of 10 months and operation revealed a depressed fracture on the left side. Right-sided hemiparesis and convulsions followed. S.E.G. at 20 months showed a ratio of 0.34, 3rd ventricle 7 mm. Left side - 10 mm. Further operation revealed a meningo-cerebral scar and this was removed. A third operation was performed at the age of 2 years 3 months. An organised haematoma with degeneration was removed. Since then he has done well and has only slight handicaps.

246.

N.K. no. 09108/52. Boy born 21.7.48. Familial predisposition: mother's brother has convulsions. Third of four children. Pregnancy normal. Delivery was precipitate and injections were given. Otherwise no complications. Birth weight 4000 g.

Symptoms: development was normal but speech was poor. At the age of 3 years he had three convulsions in which he became rigid and unconscious, ground his teeth and jerked his arms. The convulsion lasted about 10 minutes. Admitted to the R.H. Paediatric Department twice at the age of 4 years. E.E.G. showed severe dysrhythmia with a focus in the right occipital region. X-ray of skull normal.

L.E.G.: ratio 0.34 (0.29/0.37). 3rd ventricle ? Right side - 8 mm. Normal cortical air. During admission a congenital heart disorder was discovered (? ventricular septal defect).

Admitted to N.K. department at the age of 3 years 10 months. Eyes: left-sided convergent squint and amblyopia. Mental development normal but speech retarded. Head circumference 54 cm.

Right-sided arteriography: no definite abnormality but a posterior hygroma could not be excluded. No temperature or other complication after the examination. Burr hole on the right side showed no sign of hygroma.

Follow-up: patient has had only one seizure since discharge but has occasional headaches and dizziness. He attends an ordinary school, finds arithmetic difficult but talks very well. He is a very strong child. Physical examination: mental development corresponds to age. Head is large, 55.6 cm. No squint. Right-sided vision 6/6, left-sided 6/24. No neurological abnormality. Weak systolic murmur present.

Diagnosis: previous epilepsy, systolic murmur, healthy.

Summary: a boy with a family history of convulsions who himself developed seizures at the age of 3 years. L.E.G. at 4 showed a ratio of 0.34, 3rd ventricle ?, right side - 8 mm. He has been well since discharge and attends a normal school.

247.

N.K. no. 2373/41. Boy born 13.10.29. Familial predisposition: a cousin has epilepsy. Only child. Pregnancy normal. Delivery difficult and prolonged. Forceps used. Birth weight unknown. No neonatal symptoms.

Symptoms: seizures began after an uncomplicated attack of scarlet fever and increased over 3 years. He became withdrawn, flaccid and red in the face, also had palpitations and salivation and the entire convulsion lasted a few minutes. He was treated with ultra-violet light with good effect and had no more seizures until about 3-4 months before admission when they recurred. Admitted to the R.H. Neuromedical Department at the age of 11 years 2 months. L.E.G. showed displacement to the left and the right temporal horn appeared dilated. There was an air collection in the upper part of the right hemisphere.

Admitted to N.K. department at the age of 11 years 4 months. In the posterior

part of the right parietal region a 12×10 cm. bony prominence could be seen and felt. Eyes normal. X-ray of skull showed it to be thin-walled with a deep posterior fossa. On the left lateral picture the calvarium was seen to be somewhat enlarged and thin. V.E.G. pressure 230. Ratio 0.35 (0.31/0.40). 3rd ventricle 6 mm. Left side - 16 mm.

There was a large cavity in the posterior part of the right hemisphere.

Operation over the posterior part of the right hemisphere showed the dura to be adherent to the cortex over most of the hemisphere. The cortex was severely atrophic with small gyri. The dura was freed and the thin cortical area removed down to a fist-shaped ventricular cyst. This cyst was divided into two parts by a band of connective tissue which was cut. The third ventricle bulged into the lumen. Microscopy of the tissue showed scarred and atrophic brain tissue and a meningo-cerebral scar. The post-operative period was uncomplicated apart from a rise in temperature to 40°C . His temperature continued to swing for two weeks and there was a concurrent cell increase in the cerebrospinal fluid.

Follow-up: admitted to a children's hospital at the age of 10 and again at 11. Admitted to a hospital for epileptics at the age of 17 until 20. Diagnosis: brain damage at birth, intellectual inferiority, epilepsy. At first during admission there were many petit mal episodes. Four attempts at P.E.G. were made without successful filling. I.Q. at the age of 16 was 87. E.E.G. showed many waves on hyperventilation. Has been awarded an invalid pension and has apparently not had any seizures during the past five years. Continues to take phenobarbitone and phenytoin. Works as a labourer. On physical examination he appears to be both physically and mentally normal. Head circumference about 55 cm. Eyes and reflexes normal.

Diagnosis: previous epilepsy, otherwise healthy.

Summary: a boy with a family history of epilepsy and whose delivery was by forceps. Convulsions began when he was about 8 and were accompanied by headache and salivation. V.E.G. at 11 showed a ratio of 0.35, 3rd ventricle 6 mm. Left side - 16 mm. At operation a meningo-cerebral scar was found posteriorly on the right side with a large ventricular cyst extending into the scar. He receives an invalid pension but is now doing well and working as a labourer. He has had no seizures for five years and on physical examination is healthy.

248.

N.K. no. 2560/41. Boy born 6. 10. 33. No familial predisposition. First of three children. Pregnancy normal. Delivery by forceps but no asphyxia. Birth weight 3500-4000 g.

Symptoms: at the age of 21 months sustained a depressed skull fracture with bone fragments in the left parietal region. There was contusion of the dura and brain. The patient was admitted to hospital where craniotomy was performed some time after the accident. He then developed a right-sided spastic hemiplegia and 6 months later a Jacksonian-type convulsion which was followed 2-3 years later by generalised convulsions. Admitted to the R.H. Neuromedical Department where he had a generalised tonic convulsion involving the right side more than the left.

Admitted to N.K. department at the age of 7 years 11 months. On the left side of the head was a large bone defect. There was also a right-sided hemiplegia with hypoplasia. X-ray of skull showed sequelae of fracture and craniotomy. E.E.G. not performed. An examination to confirm that there was air in the ventricular system was carried out and was followed by V.E.G. ratio 0.35 (0.25/0.44). 3rd ventricle 7 mm. Right side - 5 mm. There was a collection of air over the left parietal region. Temperature 38.2°C . the day after the examination, normal on the third day. Otherwise no complications.

Follow-up: is at home and has for the past few years been completely bed-ridden. He has continued to have convulsions of varying type, chiefly generalised. He is completely helpless. There have been incidents of status epilepticus. Physical examination: is in very poor condition and appears grossly retarded. He understands nothing of what is said to him and does not say a word himself. Does not recognise his parents. Appears very small, probably no higher than 160 cm. Head circumference 59 cm. No eye signs.

There is a severe predominantly right-sided spastic tetraplegia with contractures of most joints. There is coarse, prolonged ankle clonus and bilateral Babinski.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia (right more than left), epilepsy.

Summary: a boy whose delivery was by forceps and who sustained a severe head injury at the age of 21 months. After this he developed a right-sided spastic hemiplegia and later convulsions. V.E.G. when nearly 8 years old showed a ratio of 0.35, 3rd ventricle 7 mm. Right side - 5 mm. Is at home and severely retarded. He has a predominantly right-sided spastic tetraplegia and continuing seizures.

249.

N.K. no. 7977/46. Boy born 27. 3. 34. No familial predisposition. Second of two children. Pregnancy and delivery normal. Birth weight not known.

Symptoms: he was hit on the head by a plank at the age of 7 years. For about a year after this he complained of headache, usually on the right side. Did well at school. Admitted to the R.H. Neuromedical Department and transferred.

Admitted to N.K. department at the age of 12 years. Is left-handed. Eye and neurological examination normal. X-ray of skull normal.

S.E.G.: pressure 250. Ratio 0.35 (0.32/0.38). 3rd ventricle 4 mm. Right side - 6 mm. Temperature 38.2° C. the third day, otherwise no complications.

Follow-up: the patient was not examined by the author as he is living in Germany. The family doctor wrote to say that he was completely well and is completing his training as an ironmonger. No motor or mental difficulties.

Diagnosis: healthy.

Summary: a boy who developed headaches after a head injury at the age of 7 years. S.E.G. at 12 years showed a ratio of 0.35, 3rd ventricle 4 mm. Right side - 6 mm. Is completely healthy.

250.

N.K. no. 09126a/52. Girl born 24. 2. 51. Familial predisposition: father's brother had convulsions at the age of 2 and 14 years. Second of two children. Pregnancy normal. Delivery by forceps because of threatened intrauterine asphyxia. She was, however, not asphyxiated but was very quiet with weak heart sounds. Birth weight 3100 g.

Symptoms: in connection with high fever at the age of 9 months she had generalised tonic convulsions with loss of consciousness. Admitted to hospital where sub-dural puncture showed clear fluid. Convulsions continued during admission and the patient was treated with antibiotics. Eyes normal. X-ray of skull showed raised intracranial pressure. Right-sided ankle clonus was present. E.E.G: no activity over the left hemisphere.

First admission to N.K. department at the age of 9 months. Eye examination revealed conjugate ophthalmoplegia. Head circumference 46.2 cm. Movement of right-sided extremities less than of the left side. X-ray of skull: sutures remarkably sharply outlined. E.E.G: severe dysrhythmia with severely depressed activity over the left hemisphere.

V.E.G.: clear fluid. Examination unsuccessful. Repeated three days later. Ratio 0.37 (0.34/0.41). 3rd ventricle 10 mm. Right side - 6 mm. No temperature or other complaints after the examination.

Second admission to the N.K. department at the age of a year. Had had a recurrence of convulsions and had been admitted to a paediatric department with diarrhoea and a temperature of 39.9° C. There was a right-sided spastic hemiplegia and intermittent squint. Just before admission there had been petit mal seizures. Eyes showed no abnormality apart from squint. She could sit alone but could not stand or walk. Left-sided arteriography: good filling. Anterior and media cerebri raised corresponding to ventricular dilatation.

S.E.G.: pressure 250, clear fluid. Ratio not definite measurable but on some A-P pictures could be assessed at 0.33/0.57. 3rd ventricle 11 mm. Pronounced difference between the sides on that occasion with displacement to the left. No complications after the examination.

Follow-up: has since been followed up in the Orthopaedic Hospital's cerebral palsy clinic. Lengthening of the Achilles' tendon performed with good result. Developmental quotient 100. She has been admitted on several occasions to a children's hospital. E.E.G.

showed marked depression of activity over the left hemisphere. In addition there was spike-wave activity over the right hemisphere from the age of two years. Physical examination showed a right-sided spastic hemiplegia which was more pronounced in the arm. There was also a slight convergent squint. Mental state appeared normal. On admission to a paediatric department at the age of 7 years: L.E.G. ratio 0.53 (0.28/0.84). 3rd ventricle 11 mm. pushed to the left. Left side - 12 mm.

Left-sided hemispherectomy has since been performed. The whole hemisphere was malformed and atrophic. Did well post-operatively but her condition is still largely unchanged.

Diagnosis: right-sided spastic hemiplegia, epilepsy.

Summary: a girl in whose family there was a history of convulsions. Delivery was by forceps. At the age of 9 months she developed febrile convulsions and following this a right-sided spastic hemiplegia. V.E.G. showed a ratio of 0.37, 3rd ventricle 10 mm. Right side - 6 mm. Convulsions continued and S.E.G. showed a ratio of 0.33, 3rd ventricle 11 mm. L.E.G. showed a ratio of 0.53, 3rd ventricle 11 mm. Left side - 12 mm. Left-sided hemispherectomy performed but at the time of follow-up shortly afterwards her condition was largely unchanged.

251.

N.K. no. 02336/48. Girl born 17.8.45. No familial predisposition. Third of three children. Pregnancy: vaginal discharge towards the end of the nine months as well as frequent vomiting. Delivery lasted 16 hours and was difficult. No asphyxia. Birth weight 4000 g.

Symptoms: seizures during which the patient became quite black in the face occurred at 24 hours. Treated with oxygen for four days. During that period it was noticed that she had a left-sided hemiparesis. Blindness established at 4 months, later squint. Left-sided hemiparesis had been improving particularly in the leg. Mentally she was thought to be normal but was inclined to hysterical reactions. Admitted to a paediatric department at the age of 3 years.

Transferred to N.K. department. Eyes reacted to light. Bilateral optic nerve atrophy present. Cranium small. Spastic hemiplegia particularly in the arm. E.E.G. no definite abnormality. X-ray of skull normal.

S.E.G.: pressure 300, clear fluid. Ratio 0.38 (0.42/0.36). 3rd ventricle 6 mm. Right side - 10 mm. Temperature 38.4° C. the day after the examination, afterwards normal.

Follow-up: has had occasional seizures with long intervals between and is under the care of a neuromedical department. E.E.G. is becoming normal. Is in a special school for the blind. Physical examination: head circumference 50 cm. Left-sided spastic hemiplegia. Speech is good and she plays the piano by ear very well. Gait is only slightly handicapped by hemiplegia and more by blindness and she manages well indoors. Puberty is beginning.

Diagnosis: left-sided hemiplegia, blindness, epilepsy.

Summary: a girl whose delivery was difficult and who had convulsions during the first 24 hours of life. Left-sided paresis present and blindness later established. S.E.G. at 3 years showed a ratio of 0.38, 3rd ventricle 6 mm. Right side - 10 mm. Is doing well in an institution for the blind and has only rare seizures. She is only slightly handicapped by the hemiplegia.

252.

N.K. no. 9915/47. Boy born 26.1.43. Familial predisposition: mother is feeble-minded and has been punished for incest. Father is a criminal. Of the siblings the first has been punished for thieving, the second cannot keep a job, the third and fourth are mentally deficient. Patient is fifth of the seven children (including abortions he is the eighth of ten). No information on pregnancy. Delivery normal. Birth weight unknown.

Symptoms: normal development until the age of about a year when he was admitted to a dermatological department and transferred to a paediatric department because of pulmonary tuberculosis, left-sided suppurative otitis media, cerebral tuberculoma, left-sided hemiplegia, tuberculoid keratitis and fluid in the knee joint. He was in a sanatorium

until the age of 3 years. After that he was admitted to a hospital for infectious diseases because of meningitis, an eye department because of keratitis and a neuromedical department at the age of 4 years 4 months. L.E.G. showed the ventricular system to be displaced to the right. The largest degree of dilatation was in the right lateral ventricle. He had never had convulsions.

Admitted to N.K. department at the age of 4 years 5 months. Appeared mentally retarded. Eyes: corneal opacities. There was a left-sided spastic hemiparesis, involving the arm more than the leg. X-ray of skull normal. E.E.G.: severe dysrhythmia.

S.E.G.: clear fluid. Ratio 0.39 (0.47/0.32). 3rd ventricle 11 mm. Right side - 17 mm. No temperature or other complications.

Follow-up: placed under State mental care at the age of 7 years 3 months and admitted to a State mental institution at the age of 8 years 2 months. I.Q. at the age of 5 was 62 and at 11 it was 57. E.E.G. at the age of 7 showed focal dysrhythmia maximal in the right occipital area. Has been a good-tempered and easy child. Enjoys school but results are poor. Is easy to occupy at school and in the workshop and makes no trouble. Physical examination: pleasant and co-operates well. Pronounced left-sided spastic hemiplegia, mostly in the hand. Speech and understanding are good. Head circumference 52 cm. Gait is good. Mental development appears to be better than his I.Q. would indicate.

Diagnosis: oligophrenia (debilitas mentis), left-sided spastic hemiplegia.

Summary: a boy with an exceedingly poor family history of oligophrenia and criminal tendencies. At the age of a year he had pulmonary tuberculosis and complications including a possible tuberculoma of the cerebrum and a left-sided hemiplegia. S.E.G. at 4½ years showed a ratio of 0.39, 3rd ventricle 11 mm. Right side - 17 mm. He is in a State mental institution, is an easy child to handle and enjoys school. His left-sided hemiplegia is unchanged.

253.

N.K. no. 9109b/46. Boy born 14. 12. 34. Familial predisposition: mother's sister and mother's brother are both in a mental hospital. Second of two children. Pregnancy normal. Delivery a month premature, induced. Birth weight 2500-3000 g.

Symptoms: head injury 21 months before admission. No real ill-effects. About a year later had generalised convulsions with loss of consciousness in connection with whooping-cough. To begin with they occurred about three times a day but later decreased. At the same time he was increasingly restless and naughty. Admitted to an epileptic department at the age of 6½ for 7 months and then to the R.H. Neuromedical Department for 3 months.

Admitted to N.K. department at the age of 7 years 4 months. Eyes normal. Left hand used more than the right. Doubtful slight paresis of right arm. Reflexes normal. X-ray of skull showed it to be mesocephalic and thin-walled. E.E.G. not done.

L.E.G.: performed in the Neuromedical Department. Described as fairly good filling of the system and some asymmetry. Moderate amount of surface air.

Operation over the anterior part of the left hemisphere where a typical glial scar about the size of a walnut was found. Microscopy: meningo-cerebral scar. Post-operative course uncomplicated. Second admission to the N.K. department at the age of 11 years 10 months. Had been symptom-free until 3 months before admission when he had weekly convulsions. Mental development normal until then and was doing well at school. Physical examination: eyes normal. Neurological examination normal. E.E.G. showed severe dysrhythmia with epileptic formations mostly on the left side.

S.E.G.: pressure 120, clear fluid. All the air was on the convexity and there was no air in the ventricles.

Third admission to the N.K. department two months later because of increasing convulsions and behaviour difficulties after S.E.G. Eyes unchanged. E.E.G.: moderate dysrhythmia. Discharged for medical treatment. No complications after examination.

Follow-up: admitted to a hospital for epileptics from the age of 12 to almost 13 years and for a further four months two years later. No abnormality found on neurological examination except for a single incident of doubtful slight paresis of the right side. L.E.G.: ratio 0.40 (0.32/0.48). 3rd ventricle 6 mm. Left side - 9 mm. L.E.G. at

the age of 15: ratio 0.35 (0.31/0.40). 3rd ventricle 3 mm. Left side - 11 mm. I.Q. at 8 years 91.

Visited at home and found to be living in appalling conditions. Both the patient and his mother appeared to be mentally disturbed. Speech was very indistinct and he sounded almost as though he were intoxicated. Both were in bed though it was the middle of the day and the room was very dirty. The whole examination was repeatedly interrupted by the "liberation song" played as loudly as possible on the radiogram. Work seemed to be an unknown factor. The patient has continued to have convulsions but they are now less frequent and less severe than earlier. There can be a seizure-free period of 4-5 months. He still takes anti-epileptic drugs. A complete neurological examination was not possible. The patient did not appear paretic or to have decreased function of the extremities. Head circumference 56 cm. The mother was full of reproach that the patient had been sent to the N.K. Department where she believed that half the patient's anterior brain had been removed (this she based on the finding of a depression over the supra-orbital arch), so causing his intellectual difficulties. These she does not qualify except by commenting: "What it is that makes youth today is what it is."

Diagnosis: epilepsy, ? psychopathy, ? intellectual inferiority.

Summary: a boy with a maternal family history of mental disorder. He sustained a head injury at the age of about 6 years and a year later began to have generalised convulsions and increasing behaviour problems. L.E.G. at 7 years 4 months showed an asymmetrical system. Operation revealed a meningo-cerebral scar on the left side. Convulsions increased and mental state worsened. L.E.G. at 12 years showed a ratio of 0.40. 3rd ventricle 6 mm. Left side - 6 mm. Ratio two years later was 0.35. 3rd ventricle 3 mm. Left side - 11 mm. At follow-up the patient appeared to be psychopathic and presumably retarded. Seizures continued.

254.

N.K. no. 01991/48. Girl born 7.4.47. No familial predisposition. Only child. Pregnancy normal. Delivery prolonged and difficult. Cord around the neck. Patient was asphyxiated for several minutes. Birth weight 3500 g.

Symptoms: convulsions immediately after birth and rigidity for two days. No fluid obtained on lumbar puncture. Cried a lot and would not use right hand. Motor development retarded. Admitted to a paediatric department and transferred.

Admitted to N.K. department at the age of 15 months. Head circumference 45 cm. Could not walk or talk. Right-sided spastic hemiparesis present. Eyes normal.

V.E.G.: pressure 110. The child cried during the puncture and some air was expressed but there was a large dilatation with good filling of the 3rd ventricle. The pictures were not definitely measureable but there was ventricular dilatation and some increase of surface air. Ratio 0.40 (0.36/0.45). 3rd ventricle ? Right side - 7 mm. Temperature 37.7° C. the day after, otherwise no complaints.

Follow-up: is under State mental care and since the age of 2 years has been in a State mental institution. Her spasticity is being treated and she is also beginning to talk. Right-sided subluxation of the hip was diagnosed at the age of 7 years. Physical examination: condition appeared satisfactory. Marked speech difficulty present and right convergent squint. Head circumference 51 cm. Is very rigid and has a predominantly right-sided spastic tetraplegia.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia (right more than left side).

Summary: a girl whose delivery was difficult and who was asphyxiated for several minutes. Convulsions occurred immediately after birth and motor development was retarded. There was a right-sided spastic hemiplegia. V.E.G. at 15 months showed a ratio of 0.40. Right side - 7 mm. She is in a State institution for mentally retarded, is doing fairly well and has a predominantly right-sided spastic tetraplegia.

255.

N.K. no. 23280/55. Girl born 4.4.50. No familial predisposition. Third of three children. Pregnancy: vaginal discharge during the last half of pregnancy. Delivery easy but patient was asphyxiated for an hour. Birth weight 4500 g.

Symptoms: at the age of 6 months it was noticed that she was noticeably rigid and twitched every now and then. Motor development was very slow. Admitted to the R.H. Paediatric Department at the age of 18 months. E.E.G. normal. I.Q. 39. Some progress made on physiotherapy. At the age of 4 years petit mal was observed and coarse jerks in the arms and upper half of the body. Re-admitted to the R.H. Paediatric Department at the age of 5 years. E.E.G. severely abnormal (petit mal variation). E.E.G. provoked a convulsion with spike-waves corresponding to the jerks.

L.E.G: ratio 0.40 (0.35/0.45). 3rd ventricle 6 mm. Left side -9 mm. No abnormal cortical air.

Admitted to N.K. department at the age of 5 years. Eyes: convergent squint. Head circumference 46 cm. Generalised variable increase of muscle tone. Marked spasticity. Abduction of hips to 90°. Scissor position on attempting to walk. Increased patellar reflexes and bilateral Babinski. Right-sided arteriography: no sign of hygroma. No complications after the examination.

Follow-up: admitted to a State mental institution at the age of 5½ years, and died there four months later. There had been daily petit mal seizures during admission and the month before she died increasing convulsions. She developed fever and a sore throat and there was dullness on percussion of the right side of the chest. Fever increased in spite of antibiotics. Death certificate diagnosis: bronchopneumonia, oligophrenia (idiocy), spastic tetraplegia. No autopsy.

Diagnosis: oligophrenia (idiocy), spastic tetraplegia, epilepsy.

Summary: a girl who was severely asphyxiated at birth and whose delivery was prolonged. From the age of 6 months she was noticed to be spastic and severely mentally retarded and petit mal seizures were observed later. L.E.G. at 5 years showed a ratio of 0.40, 3rd ventricle 6 mm., left side -9 mm. Admitted to a State mental institution and died there from a febrile disorder when almost 6 years old.

256.

N.K. no. 23469a/55. Boy born 15.11.54. No known familial predisposition. Second of two children. Pregnancy: oedema of legs, otherwise no complications. Delivery easy but patient was severely asphyxiated. Cried first after 20 minutes. Treated with swinging, bathing and injections. Birth weight 3750 g.

Symptoms: first cried properly after about 40 hours. Developed convulsions and a temperature of 38.2° C. and was admitted to hospital where neck stiffness was found. Treated with antibiotics. Cries were cerebral in character. Admitted to R.H. Paediatric Department at the age of 3 months where rigidity was found together with abductor spasms and generalised brisk tendon reflexes. Sub-dural puncture normal. E.E.G. abnormal. Possible depression of activity over the right hemisphere. Re-admitted to R.H. Paediatric Department several months later for neurosurgical examination. Physical examination: convergent squint. Rigid, spastic extremities. E.E.G. normal. X-ray of skull normal.

Admitted to N.K. department at the age of 7 months. Examination not carried out because of fever.

Re-admitted 3 weeks later.

V.E.G: bleeding from a large cortical vein on the right side. Pressure 200, clear fluid. Ratio 0.40 (0.37/0.44). 3rd ventricle 10 mm. Left side -6 mm. Marked increase of cortical air particularly frontally and in the centre. Temperature 40° C. the second day, otherwise no complications. During the examination he became pale with a rapid pulse and had to be given plasma substitute and blood. Left side had to be opened and emptied of a small haematoma and a quantity of air. Biopsy from left side showed normal cortex.

Follow-up: examined in the R.H. Paediatric Out-patient Department at the age of 10 months. There had been some progress in that there had been no seizures but the patient still seemed very stiff and his head circumference was only 44 cm. Admitted to hospital and died there at the age of 14 months from bronchitis and pneumonia with a temperature of 41.5° C. Diagnosis: capillary bronchitis. No autopsy.

Diagnosis: spastic tetraplegia, epilepsy, oligophrenia (? degree), microcephaly.

Summary: a boy who was asphyxiated for more than 20 minutes and who developed convulsions and rigidity in the neonatal period. V.E.G. at 7 months showed a ratio of 0.40, 3rd ventricle 10 mm. Left side - 6 mm. Collapsed during the procedure. After a period of progress he developed high fever and died from capillary bronchitis at the age of 14 months.

257.

N.K. no. 00993a/47. Boy born 17. 5. 46. No familial predisposition. Only child. Pregnancy normal. Delivery easy, 3 weeks premature. Birth weight 2200 g.

Symptoms: crying since birth. At 4 months bilateral cataract was found and operated on. Microcephaly observed at that time. Mental and physical development was retarded and at the age of a year the patient developed convulsions during which he bent his arms and both his arms and legs jerked. The seizures occurred frequently but were brief.

First admission to N.K. department at the age of 19 months. Eyes: aimless eye movements. Aphakia on both sides. Head circumference 42 cm. Could not walk and could not stand alone. Bilateral Babinski. X-ray of skull: increased digital markings posteriorly, otherwise no abnormality. Mental development appeared retarded.

V.E.G: pressure 80. Ratio 0.42 (0.46/0.38). 3rd ventricle 5 mm. Right side - 11 mm. Temperature 38.2° C. the same day, 38.8° C. the next day, thereafter normal. Formation of granulation tissue with pus.

Second admission to N.K. department 3 weeks later because of infection in the burr holes. This cleared up well. No further examinations performed.

Follow-up: admitted to a State mental institution at the age of 23 months, where he stayed until his death two years later. Physical examination on admission revealed a spastic tetraplegia, mostly in the legs. Eyes showed artificial atrophy and sequelae of cataract operation. Occasional petit mal seizures noticed. There was a rise in temperature and a sore throat just before his death. Diagnosis: tonsillitis complicated by bronchopneumonia, encephalopathy and epilepsy. Death certificate diagnosis: bronchopneumonia. No autopsy.

Diagnosis: oligophrenia (idiocy), microcephaly, spastic tetraplegia, bilateral cataract (operated on), epilepsy.

Summary: a boy born 3 weeks prematurely. Bilateral cataract noticed at 4 months. Mental and physical development retarded and head circumference small. Convulsions developed at the age of a year. V.E.G. at 19 months showed a ratio of 0.42, 3rd ventricle 5 mm. Right side - 11 mm. Placed in a State mental institution where he died at the age of 4 years from bronchopneumonia. Spastic tetraplegia present and seizures had continued.

258.

N.K. no. 05900a/50. Boy born 21. 12. 43. No known familial predisposition. Only child. Pregnancy normal. Delivery by breech presentation. Birth weight 3000 g.

Symptoms: admitted to a nursery immediately after birth. Was very poorly at the age of a month and was admitted to hospital because of possible intracranial haemorrhage. Squint from the age of a year. After that he was well until about the age of 4 years when he had a convulsion while asleep with clonic jerks in the left arm. Re-admitted to hospital where he had a minor seizure. Examined by the neurologists because of a possible brain tumour.

Admitted to N.K. department at the age of 4 years. Eyes: left divergent squint. X-ray of skull: venous markings increased in the parietal region.

V.E.G: pressure 120, clear fluid. No definitely measurable A-P pictures but measured on the temporal horn pictures the ratio was 0.43 (0.49/0.37). 3rd ventricle 14 mm. On that picture the left side was - 6 mm. Temperature 38.5° C. the day after, otherwise no complaints.

Second admission to N.K. department at the age of 6½ years. Had had 3 seizures

since the last admission. Eyes: left divergent squint. Slightly reduced reaction of the left facial nerve. Left-sided spastic hemiplegia most pronounced in the arm. E.E.G.: severe dysrhythmia with marked localisation to the right temporal region. X-ray of skull unchanged. Mental state normal.

S.E.G.: pressure 350, clear fluid. Ratio 0.55/0.38. 3rd ventricle ? Right side - 5 mm. No temperature or other complaints after the examination.

Operation over the right hemisphere. Parasagittally in front and behind the central sulcus was found an atrophic lesion with pale gyri and increased fluid collection. Cortex otherwise looked normal. No activity over the atrophic lesion and it was removed. Microscopy: congenital cerebral dysplasia. Temperature 39.1° C., otherwise no complications post-operatively.

Follow-up: seen as an out-patient in the Orthopaedic Hospital's cerebral palsy clinic: cerebral palsy, spastic hemiplegia. Treatment almost unnecessary but arm exercises given. E.E.G. at the age of 10 years was severely abnormal with numerous low frequencies. He had done well since his operation. Memory not very good and attends a special school and does well. Began school rather late. Physical examination: head circumference 55.2 cm. Eyes normal. Marked left-sided hemiplegia. Intellectually appeared normal. Normal, healthy appearance.

Diagnosis: left-sided spastic hemiplegia.

Summary: a boy who was delivered by breech presentation and who made no progress during the first month of life. At the age of 4 he had convulsions localised to the left arm. V.E.G. almost 3 years later because of more seizures showed a ratio of 0.55/0.38. Right side - 5 mm. Operation over the right hemisphere showed an atrophic lesion which was removed. Attends a special school. Has no seizures and is not troubled by the left-sided hemiplegia.

259.

N.K. no. 08230a/51. Yugoslavian girl born 14.8.44. No known familial predisposition. Only child. No information on pregnancy or birth. Delivery difficult, lasted 14-15 hours. Birth weight not known.

Symptoms: rigidity of the right hand and uncertainty of movement of the right arm since the age of 3 months. At the age of 4 months there were occasional right-sided facial jerks. No further seizures. Had always dragged right foot and appeared mentally and physically considerably retarded. Walked at 17 months. Talked at 3 years. Always nervous, irritable and sensitive.

First admission to N.K. department at the age of 7 years. Healthy appearance. Eyes normal. Head circumference 49.5 cm. Rather difficult to make contact with (? language difficulty). Intelligence difficult to assess but possibly a little reduced. Right-sided spastic hemiplegia involving the arm more than the leg. Left-sided arteriography showed no abnormality.

V.E.G.: pressure 20. Ratio 0.43 (0.28/0.60). 3rd ventricle 11 mm. Left side - 7 mm. Temperature 39° C. the same day, normal six days later. No other complications. Microscopy of cortex showed slight artificial changes.

Second admission to N.K. department at the age of 7 years 3 months. Had been treated with glutamic acid without effect. Seizures still seen on admission. Eyes normal. Reflexes very brisk in the right arm. No further investigations undertaken.

Follow-up: was only followed up for a short time until the age of 7 years 5 months. E.E.G. continued to show dysrhythmia but was less abnormal than previously. The patient had improved in that she had ceased to have convulsions during the last few months. The family emigrated to U.S.A. via France and no information has been obtainable since.

Diagnosis: epilepsy, right-sided spastic hemiplegia.

Summary: a girl whose delivery was difficult and who developed a right-sided spastic hemiplegia during the first month of life. Localised convulsions occurred at 4 months and development was retarded. V.E.G. at 7 years showed a ratio of 0.43, 3rd ventricle 11 mm. Left side - 7 mm. Followed up for only a short time because of emigration but she appeared to have made some progress and seizures had ceased.

260.

N.K. no. 22708/54. Girl born 2. 4. 41. Familial predisposition: mother had syphilis. Third of three children. Pregnancy and delivery normal. Birth weight 3270 g. Mother's syphilis was not diagnosed at time of child's birth.

Symptoms: positive W.R. established at 12-13 months of age. Walked alone at 12-13 months and began to talk at the same time. Salversan treatment started when nearly 2 years old. About a year later, after a salversan injection, the patient was found deeply comatose in bed that night. Admitted to hospital where she remained unconscious for a week and developed a right-sided paresis. This improved slowly on physiotherapy. Mental development was retarded after the period of unconsciousness.

From the age of 3 she had Jacksonian-type seizures with paraesthesiae in the right arm followed by rigidity of the entire right side of the body. They lasted 30-60 seconds and afterwards she was tired and apathetic. Seizures occurred 1-20 times a week. Mentality was infantile and she had to have special teaching. The hemiparesis improved a great deal until she could both stand and walk.

Admitted to N.K. department at the age of 13 years 7 months. Eyes: sequelae of syphilitic choroiditis. Right-sided facial paresis, right-sided spastic hemiplegia involving the arm more than the leg. Deep sensory response and stereognostic sense reduced on the right. Right-sided Babinski. E.E.G.: spike focus in the left occipital region. X-ray of skull normal.

S.E.G.: pressure 370. Ratio 0.43 (0.36/0.52). 3rd ventricle 8 mm. Left side—12 mm. Increased cortical air on the left side. Temperature 38.1° C. the day after, otherwise no complications.

Left-sided arteriography: carotid normally filled. Anterior cerebral artery raised corresponding to the ventricular dilatation. It appeared as though the terminal vessel was depressed. There was presumably an emboli in the left media cerebral artery and hemispherectomy was considered.

Follow-up: seizures continue and may occur 7 times during 24 hours. The right side is entirely rigid and the left side jerks. Hardly uses right hand and gait is somewhat unsteady. Cannot walk for more than half an hour. Is being taught at home. Can dress herself and eat and drink without help. Takes anti-epileptic drugs and has physiotherapy. Physical examination: mental development approximately corresponds to age and I.Q. is thought to be about 70. Eyes: convergent squint. Right-sided spastic hemiplegia, particularly severe in the arm. Head circumference 51 cm.

Diagnosis: right-sided spastic hemiplegia, epilepsy, intellectual inferiority (? debilitas mentis).

Summary: a girl who has congenital syphilis. Under treatment with Salversan she had a possible emboli with consequent coma and right-sided hemiplegia. Jacksonian-type epilepsy followed and S.E.G. was performed at 13 years 7 months. Ratio 0.43, 3rd ventricle 8 mm. Left side - 12 mm. Seizures continue and she is handicapped by spastic hemiplegia and some mental retardation.

261.

N.K. no. 24029a/55. Boy born 12. 12. 53. Familial predisposition: father's brother and mother's sister both have epilepsy. Fourth of four children. Pregnancy complicated by pyelitis and albuminuria. Delivery: child in transverse position. Caesarian section performed. No asphyxia. Birth weight 3050 g.

Symptoms: was flaccid and would not take the breast for the first few days of life. Motor development was retarded and at 4 months it was noticed that the right arm and leg were being moved very little. He was 6 months old before he raised his head while lying on his back. Admitted to the R.H. Paediatric Department at the age of 14 months. E.E.G. showed no definite abnormality. L.E.G.: atrophic lesion of the mixed type. Ratio 0.41 (0.37/0.44). Increased basal air but no surface air.

Admitted to N.K. department at 16 months. Eyes normal. Appeared somewhat mentally retarded. Used the left hand. Slight right-sided spastic hemiplegia present. E.E.G.: no

definite abnormality seen. X-ray of skull normal. Transferred to surgical department for removal of a dermoid cyst.

Re-admitted 10 days later.

V.E.G. ratio 0.44 (0.40/0.47). 3rd ventricle 7 mm. Right side - 6 mm. Temperature 38.4° C. the day after, normal on the third day. Otherwise no complications.

Follow-up: has since been followed up in the R.H. Paediatric Out-Patient Department. Has occasional generalised convulsions. Has a strange right-sided hemiplegia, almost flaccid with a right-sided facial paresis. The shape of the head is very asymmetrical with flattening at the back on the right. Does not talk very much but understands fairly well. Salivates a great deal. E.E.G. shows a severely abnormal curve. Eyes: condition as before, pseudo-neuritic disc findings. Otherwise no abnormality. Developmental quotient at the age of 6 was 47. *Left-sided hemispherectomy* has been performed recently. An atrophic hemisphere with cystic changes was found. Still no real change in the patient's condition.

Diagnosis: epilepsy, oligophrenia (imbecility), ? right-sided spastic hemiplegia.

Summary: a boy with a family history of epilepsy. Pregnancy was complicated by pyelitis and delivery was by Caesarian section. Had symptoms from the first few days of life and development was retarded. Spastic hemiplegia noted and L.E.G. performed. Ratio 0.41. V.E.G. at 16 months showed a ratio of 0.44, 3rd ventricle 7 mm. Right side - 6 mm. Hemispherectomy has been performed recently but so far there is very little change in the condition.

262.

N.K. no. 23451/55. Boy born 7.5.54. No familial predisposition. Fourth of four children. Pregnancy and delivery normal. Birth weight 3700 g.

Symptoms: no symptoms neonatally and though motor development was slow a doctor was not consulted until the child was 6 months old. Examined at the R.H. Paediatric Department at the age of 9 months. Could not sit or grasp objects and did not recognise his parents. Head circumference 48.2 cm. X-ray of skull, eye examination and E.E.G. normal.

Admitted to N.K. department at the age of 13 months. E.E.G. severely abnormal with spikes in the left occipito-temporal region. Depression of activity on the right side.

S.E.G. pressure 300, clear fluid. No filling of the ventricles.

V.E.G. pressure 200, clear fluid. Ratio 0.50 (0.40/0.59). Right side - 13 mm. 3rd ventricle 14 mm. Surface air altered position between the two examinations. After S.E.G. his temperature was 39.1° C. but was normal the next day. After V.E.G. it was 38.7° C. and he was still febrile on discharge three days later. Otherwise no complications.

Follow-up: has since been followed up as an out-patient in the R.H. Paediatric Department. Has had frequent febrile episodes but no seizures. His understanding has improved and now at the age of 3 years he can walk in a walking-chair but he does not use his hands. He can presumably understand what is said to him but he says only single words himself. There is coarse, prolonged bilateral ankle clonus, variable muscle tone and atypical Babinski. He has had no real seizures but there have been two episodes of collapse which have lasted two hours. Head circumference at the age of 20 months was 43.4 cm. Application for the child to be placed under State mental care has been postponed but will presumably eventually become necessary.

Diagnosis: spastic tetraplegia, oligophrenia (? debilitas mentis, ? imbecility).

Summary: a boy whose development was slow from birth. V.E.G. at 13 months showed a ratio of 0.50, 3rd ventricle 14 mm., right side - 13 mm. At follow-up he was found to be severely handicapped by spastic tetraplegia and mentally retarded.

263.

N.K. no. 5284/44. Girl born 6.9.39. No familial predisposition. First of two children. Pregnancy and delivery normal. Birth weight unknown.

Symptoms: discharge from the left ear. At the age of 4 years she was treated orthopaedically for pes planus and valgus. A minor head injury about a year before admission was followed by increasingly uncertain and broad-based gait and a tendency

to fall. During the 9 months prior to admission there had been tremor of the arms and legs, she had become fat, sleepy and irritable. Admitted to a children's hospital for 3 months at the age of 4½ years followed by admission to the R.H. Neuromedical Department. L.E.G. described the lateral ventricles as being grossly dilated, the left more than the right.

Admitted to N.K. department at the age of 4 years 8 months. Eyes normal. Gait broad-based. Positive Romberg. Bilateral Babinski. Patellar reflexes brisk on both sides. X-ray of skull and E.E.G. not performed.

V.E.G.: pressure 80. Ratio 0.51 (0.47/0.55). 3rd ventricle 12 mm. Right side - 6 mm. Temperature 37.9° C. the day after, normal the next day. Otherwise no complications.

Follow-up: placed under State mental care and admitted to a State mental institution at the age of 10 years and died there four months later. Diagnosis: imbecility, encephalopathy, hydrocephalus. Was very apathetic during admission, said only single words and had contractures of all her joints. Was completely helpless. Just before she died there were several episodes of high evening temperature but no abnormality was seen on physical examination and no seizures. Died in hyperpyrexia. No autopsy.

Diagnosis: oligophrenia (imbecility), spastic tetraplegia.

Summary: a girl who sustained a minor head injury at the age of about 3½ years. This was followed by increasing gait difficulties, tremor, obesity and irritability. *V.E.G.* at 4 years 8 months showed a ratio of 0.51, 3rd ventricle 12 mm., right side - 6 mm. She was admitted to a State mental institution and died there at the age of 10 years 4 months in hyperpyrexia.

264.

N.K. no. 6601/45. Boy born 3.1.34. No familial predisposition. Third of three children. No information on pregnancy. Delivery normal. Birth weight 4875 g.

Symptoms: convulsions since birth, in first 24 hours in left arm and left side of face and later also involving the right side. Admitted to a paediatric department where blood-stained cerebrospinal fluid was found. Seizures continued and at the age of 7 years he was admitted to the R.H. Neuromedical Department. L.E.G. showed no air in the ventricles. Admitted to a psychiatric department where petit mal seizures were seen. L.E.G. showed severe hydrocephalus, most marked on the left side with incomplete ventricular filling.

Admitted to N.K. department at the age of 11 years 4 months. Appeared oligophrenic. Eyes normal. Left arm shorter than right. Gait hemiplegic on the left side. Reflex changes corresponded to a left-sided spastic hemiplegia.

V.E.G.: pressure 100, clear fluid. Ratio 0.51 (0.65/0.40). 3rd ventricle 4 mm. Right side - 18 mm. Obvious arachnoiditis could be seen through the burr holes. Temperature 38° C. the day after, otherwise no complications.

Follow-up: admitted to a State mental institution at the age of 16 years 7 months. Diagnosis: imbecility, epilepsy, hydrocephalus, traumatic encephalopathy. I.Q. fell from 78 at the age of 7 to 65 at 11 to 52 at 15. On admission he was pleasant and co-operative and toilet-trained. He had many convulsions at irregular intervals. Later became somewhat aggressive and troublesome. Was very stolid. Continued to have seizures up to 12 times a month. Physical examination: a friendly but somewhat infantile boy. No deformities. Cannot occupy himself but likes to play. Talks well but does not answer simple questions adequately. Head circumference 54 cm. Eyes normal. Neurological examination normal.

Diagnosis: oligophrenia (imbecility), epilepsy.

Summary: a boy who had convulsions from birth. *V.E.G.* at 11 years 4 months showed a ratio of 0.51, 3rd ventricle 4 mm. Right side - 18 mm. Arachnoiditis seen through burr holes. Is in a State mental institution with an I.Q. of about 50. Seizures continue and he cannot work.

265.

N.K. no. 04092/49. Boy born 2.9.48. Familial predisposition: at the age of 15-17 the child's father had three epileptic seizures with loss of consciousness. Second of two

children. Pregnancy normal. Birth: cord round neck and child was cyanosed. Cried very quickly, however. Birth weight 4000 g.

Symptoms: was rigid for the first few days of life. At the age of 8 months it was noticed that he did not use his left arm. Admitted to the R.H. Paediatric Department for 3 months at the age of 10 months and a spastic paresis of the left arm found. X-ray of skull and eye examination normal.

Admitted to N.K. department at 11 months. Slight left-sided hypoplasia of the face. Left-sided spastic hemiplegia, arm more involved than leg. Left-sided Babinski. X-ray of skull normal.

S.E.G.: pressure 180. Ratio 0.52 (0.94/0.34). 3rd ventricle 4 mm. No surface air. Right side - 10 mm. Temperature 38.6° C. the day after, otherwise no complications.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. He had one epileptic seizure at the age of 3 years. He has been treated for his left-sided hemiplegia. Mental development was satisfactory. Died at home at the age of 5 years 4 months during a convulsion.

Diagnosis: left-sided hemiplegia, epilepsy.

Summary: a boy whose father had had convulsions. Delivery was difficult and he was cyanosed. Left-sided hemiplegia present from 8 months. S.E.G. at 11 months showed a ratio of 0.52, 3rd ventricle 4 mm. Right side - 10 mm. He died at home during a convulsion at the age of 5 years 4 months.

266.

N.K. no. 06824/51. Girl born 23.2.50. Familial predisposition: mother had encephalitis at the age of 5 years after vaccination. Mother's brother died at 3½ years from vaccinal encephalitis and yet another member of the family became mentally deficient after the same complication. Parents are first cousins. A brother four years older than the patient has the same clinical picture. Patient is fourth of four children. Pregnancy and delivery normal. Birth weight 3300 g.

Symptoms: respiratory difficulties and cyanosis immediately after birth. Admitted to the R.H. Paediatric Department where 4 ml. of slimy fluid were aspirated from the upper respiratory tract. Episodes of cyanosis continued during the first weeks of life. On discharge continued to be very apathetic and development was retarded. She deteriorated even more after various infections at about the age of 8 months and had generalised febrile convulsions. During the month before admission she had petit mal seizures. Admitted to the R.H. Paediatric Department at the age of 11 months and no definite abnormality found on E.E.G.

Admitted to N.K. department at 11 months. Very retarded mentally and physically. Head circumference 44 cm. Eyes: no definite abnormality. Did not smile and was markedly hypotonic. Patellar reflexes weak but elicited from entire tibial area. Bilateral Babinski.

S.E.G.: pressure 300, clear fluid. Ratio 0.52 (0.45/0.59). Right side - 5 mm. No cortical changes. No fever or other complications after the examination.

Follow-up: admitted to a State mental institution at the age of 3 years. Diagnosed as an idiot. Seizures continued during admission. She was treated with thyroid hormone for a while as she was thought to have myxoedema and X-ray of bone centres showed retarded development but no other definite abnormality. Physical examination: big, strong child; rather fat. Head circumference 49.2 cm. No co-operation or contact. Eyes: no definite abnormality seen. Reflexes brisk, particularly on the left.

Diagnosis: oligophrenia (idiotcy), epilepsy.

Summary: a girl in whose family there had been many instances of brain disorder following vaccination. An older brother is mentally retarded. The patient had immediate respiratory difficulties and was retarded from the first few weeks of life. Generalised convulsions occurred at 8 months. S.E.G. at 11 months showed a ratio of 0.52. Right side - 5 mm. Is in a State mental institution and has been treated for suspected myxoedema. Continues to have seizures.

267.

N.K. no. 09057/52. Girl born 1. 6. 49. No familial predisposition. Fourth of four children. Pregnancy: no movements felt. Otherwise no complications. Delivery was premature and precipitate. Placenta was small. Birth weight 1800 g.

Symptoms: had great difficulty with feeding from birth and was cyanotic. Admitted to a paediatric department at the age of a month because of prematurity and retarded development. Re-admitted at 9 months because of Little's disease. Eye examination showed possible atrophy of the optic nerve. Episodes of flaccidity and colour change occurred at intervals and on admission to the R.H. Paediatric Department at the age of 2 years 8 months she appeared severely mentally retarded. E.E.G.: possible lesion in the right hemisphere. X-ray of skull normal.

Admitted to N.K. department at the age of 2 years 10 months. Appeared imbecile. Eyes: convergent squint on the right and slight nystagmus. Could not sit or stand. Head circumference 44 cm. Legs atrophic and in scissor position. Very brisk patellar reflexes and ankle clonus. No Babinski. E.E.G.: severe depression of activity over the right hemisphere particularly occipito-temporally.

S.E.G.: pressure 400. Ratio 0.54 (0.66/0.40). 3rd ventricle 10 mm. Left side -9 mm. There was a certain amount of surface air. Temperature 38.9° C. the day after but she was also febrile before the examination. Otherwise no complications apart from a continuing unstable temperature.

Follow-up: has been in a State mental institution since the age of 3 years 3 months. Has had generalised convulsions as well as left-sided convulsions. E.E.G. shows severe diffuse dysrhythmia. Admitted to a children's hospital at the age of 6 years 8 months for investigation of possible precocious puberty but this was not confirmed. Physical examination: legs in frog position and obviously spastic. Ankle clonus and Babinski.

Diagnosis: oligophrenia (idiocy), spastic paraplegia, epilepsy.

Summary: a girl who was premature and had neonatal symptoms. Development was retarded and spasticity was diagnosed at 9 months. S.E.G. at 2 years 10 months showed a ratio of 0.54, 3rd ventricle 10 mm. Left side -9 mm. She is in a State mental institution and has convulsions. Her legs are spastic and she is severely mentally retarded.

268.

N.K. no. 23270/55. Girl born 8. 4. 54. No familial predisposition. Second of two children. Pregnancy normal. Delivery proceeded normally but child did not cry properly until four hours later. Birth weight 3250 g.

Symptoms: 5-10 tonic convulsions when 36 hours old. Admitted to a paediatric department where the cerebrospinal fluid was found to be yellow with a positive Pandy reaction and increased albumin. Mental and physical development retarded and extremities rigid. The left side was more affected than the right. Treated as an out-patient in the R.H. Paediatric Department. E.E.G. showed a severely abnormal curve. X-ray of skull normal.

Admitted to N.K. department at the age of 13 months. Very retarded. Head circumference 40 cm. Eyes: convergent squint. Spastic tetraplegia, most marked in the left arm. Hip and knee contractures present.

V.E.G.: pressure 25, clear fluid. Ratio 0.55 (0.46/0.66). 3rd ventricle 12 mm. Left side -12 mm. Increased cortical air on both sides. Temperature 38.8° C. the day after, otherwise no complications. Dural microscopy showed proliferation of the inner capillary layer (? outer membrane or stasis hypertrophy).

Follow-up: placed under State mental care. Followed up as an out-patient until admission at the age of 2 years. Very low-grade mental defective. Difficult to handle and having many petit mal seizures a day. Physical examination: severe spastic tetraplegia. Head circumference 40.5 cm. Condition deteriorating. Contractures of both arms and legs. Died at the age of 2 years 5 months in hospital after refusing food for many weeks. Autopsy: cerebral polyporencephaly.

Diagnosis: spastic tetraplegia, microcephaly, epilepsy, oligophrenia (idiocy).

Summary: a girl who had convulsions during the first few days of life. Development

was retarded and V.E.G. at 13 months showed a ratio of 0.55, 3rd ventricle 12 mm. Left side—12 mm. Microscopy from dura showed proliferation from capillary layer. At follow-up she had been under State mental care and died in hospital at the age of 2 years 5 months after refusing to eat. Autopsy showed cerebral polyporencephaly.

269.

N.K. no. 23001/55. Boy born 28.9.46. No known familial predisposition. Second of three children. Pregnancy and delivery normal. Birth weight 4100 g.

Symptoms: was severely jaundiced from birth and this was later revealed to be due to Rhesus immunisation. Was very sleepy for several days. At the age of 5 months his head was noticed to be very large and motor development retarded. From the age of a year the left arm and leg movements were uncertain and groping. At the age of 2 years there was an episode of unexplained unconsciousness. At the age of 6 years he suddenly became pale and dizzy and several similar episodes followed. Attended as an out-patient in the R.H. Paediatric Department. Head circumference at age of 10 years 61 cm. Two weeks before admission he had a temperature of 40.3° C. and was unconscious with clonic left-sided convulsions. This was followed by severe paresis of the left arm and leg.

Admitted to N.K. department at the age of 10 years 5 months. Head large. Eyes normal. Severe spastic paresis of left arm and to a lesser degree of the left leg. E.E.G. severely abnormal.

S.E.G.: ratio not measureable on the right side. 0.51 on the left side. Temperature 38.2° C. the third day, otherwise no complications.

V.E.G.: ratio 0.60 (0.64/0.51). 3rd ventricle? Left side—48 mm.

Right-sided arteriography: enormous bow-shaped displacement of anterior cerebral artery corresponding to possible cyst formation. *Operation* over the anterior and middle part of the right hemisphere. Cortex in frontal region atrophic. Anteriorly was found a large arachnoid or traumatic cyst which occupied the whole of the frontal lobe area. After the cyst and atrophic tissue were removed the rest of the brain appeared essentially normal. No immediate post-operative complications. Microscopy showed an arachnoid cyst. Shortly after there was spasticity of the left arm and ligation of the right anterior choroidal artery was performed. Condition was unchanged on discharge two weeks later.

Follow-up: followed up as an out-patient in the R.H. Paediatric Department. Good progress of motor development. No seizures. Head circumference 61.6 cm. Increased reflexes in the right leg. Mental state normal. E.E.G. unchanged.

Diagnosis: left-sided spastic hemiplegia, epilepsy.

Summary: a boy who had jaundice due to Rhesus immunisation and who was noticed to have a large head at 5 months. Left-sided spastic hemiplegia noticed at the age of a year and episodes of loss of consciousness since the age of 2 years. Left-sided convulsions occurred at the age of about 10 years. V.E.G. showed a ratio of 0.60, 3rd ventricle ?, left side—48 mm. Operation revealed a large arachnoid cyst occupying the entire frontal lobe. This was removed. He has since done well. He has had no seizures and is intellectually well-developed. His left-sided spastic hemiplegia continues.

270.

N.K. 08426/51. Boy born 13.9.38. Familial predisposition: mother's father had epilepsy. Only child. Pregnancy: albuminuria. Admitted from the second to the fifth month because of vomiting. Delivery normal. Birth weight 3200 g.

Symptoms: paresis of right arm discovered at 4 months and decreased vision two months later. Sight gradually returned from the age of a year onwards. At 18 months he had an epileptic seizure and was admitted to hospital. Spastic paresis of right arm present. X-ray of skull showed internal hydrocephalus. From the age of about one year until he was 8 years old he had a total of 5–6 convulsions. Did well at school.

Admitted to N.K. department at the age of 13 years 3 months. Unable to look upwards. Constant horizontal nystagmus present. Right-sided spastic paresis. E.E.G.: severe dysrhythmia localised to the left hemisphere. X-ray of skull normal.

V.E.G.: pressure 0, clear fluid. Ratio 0.65 (0.31/0.89). Right side—25 mm. 3rd

ventricle not measureable. No surface air. Temperature 38.6° C. the same day, normal on the second day. No other complications.

Follow-up: did well at school and left at normal time. Has since helped in his father's shop, looked after the till, served and written all the bills. Works thoroughly and conscientiously. Is an easy, even-tempered and contented person. Examined at the Orthopaedic Hospital at the age of 17 and found to be intellectually well-developed. It was suggested that he took a commercial course at a later time. Diagnosis: cerebral palsy, possibly of congenital foetal origin, possibly a sequelae of thrombosis, right spastic hemiplegia primarily involving the arm. Has since had operations on hamstrings and Achilles tendon. Has been seizure-free since the age of 8 years. Vocational testing has shown a strong ambition to obtain results in the directions in which he feels he can achieve, i.e. in a shop or office. Physical examination: head circumference 57.2 cm. Marked right-sided hemiplegia (also ankle clonus on the left side). Horizontal nystagmus. Reduced stereognostic sense on the right side. Appeared mentally a little slow but not retarded. Appears sensible and well-adjusted to his handicap.

Diagnosis: right-sided spastic hemiplegia, previous epilepsy.

Summary: a boy whose mother had albuminuria during pregnancy. Paresis of right arm seen at 4 months and an epileptic seizure occurred at 18 months. V.E.G. at 13 years showed a ratio of 0.65, right side -25 mm. 3rd ventricle not measureable. Has done very well in spite of his right-sided hemiplegia and is helping in the family business. He is well-adjusted to his handicap and is intellectually entirely normal.

271.

N.K. no. 23272/55. Girl born 3.3.55. Familial predisposition: mother's mother mentally disturbed and died at 40 years of age. Second of two children. Pregnancy normal. Delivery two months premature, very fast with protrusion of cord. Shortly afterwards she came blue and flaccid. Birth weight 1700 g.

Symptoms: admitted the day after birth because of low weight and cyanosis. After discharge the patient had a gastro-intestinal disturbance with diarrhoea and vomiting and was therefore re-admitted. Was severely dehydrated and ill. At the age of 6 weeks she had convulsions and opisthotonus. Temperature was 40° C. Lumbar puncture showed bloodstained fluid. Seizures increased and there was a squint and nystagmus.

Admitted to N.K. department at the age of two months. Eyes normal. Fontanelles somewhat bulging. Neurological examination showed no definite abnormality. There was an obvious "cracked pot" sound on cranial percussion. Head circumference 37.2 cm. E.E.G. severely abnormal. X-ray of skull not done. Puncture of fontanelles on both sides showed that at a depth of 1 cm. there was a hygroma from which was aspirated 25 ml. of chestnut-brown fluid.

V.E.G.: slightly xanthochrome fluid. Pressure 50. Ratio 0.80 (0.73/0.86). Right side -5 mm. 3rd ventricle about 10 mm. Remarkable distance between the lateral ventricles. ? a non-communicating septum cyst. No complications after the examination.

Follow-up: admitted to a hospital for epileptics at the age of 6 months until she died five months later with signs of bronchitis and aspiration pneumonia. Autopsy: head circumference 64 cm. No changes of pneumonia. At autopsy was found a typical picture of a severe internal hydrocephalus with two litres of clear, colourless fluid. It was not possible to pass through the Sylvian aqueduct. The brain tissue was several millimetres thick. Autopsy diagnosis: stenosis of cerebral aqueduct, severe degree of internal hydrocephalus, capillary bronchitis, aspiration of alimentary contents, scattered atelectases of the lungs and obstruction of the lungs.

Diagnosis: oligophrenia (? degree), epilepsy.

Summary: a girl who was born two months prematurely and who had neonatal cyanosis and flaccidity. A gastro-intestinal disorder was followed by severe dehydration and convulsions at the age of 6 weeks. V.E.G. at two months showed a ratio of 0.80, right side -5 mm., 3rd ventricle about 10 mm. Admitted to a hospital for epileptics where she died at the age of 11 months from a lung disorder.

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Abbreviations in conformity with the Quarterly Cumulative Index Medicus.

(The figures in brackets indicate the pages in the present work on which the respective author has been cited.)

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From the Cardiological (Chief: H. Gøtzsche, M.D.), Paediatric (Chief: Professor Bent Andersen, M.D.) and Radiological (Chief: E. Mosekilde, M.D.) Clinics of the University Hospital, Aarhus, Denmark.

CONGENITAL HEART DISEASE IN CHILDREN UNDER TWO YEARS OF AGE

A DIAGNOSTIC SURVEY WITH SPECIAL REFERENCE
TO CARDIAC CATHETERISATION AND CINE-ANGIO-
CARDIOGRAPHY USED IN A SERIES OF CONSECUTIVE
CASES

By

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During recent years, various investigators have emphasised the importance of improved methods in the diagnosis of congenital heart disease in infancy (Boesen and Vendel, 1955; Adams, 1957). If left untreated, these diseases will often lead to death during the first year of life (Warburg, 1949; Gardiner and Keith, 1951; Callensee, 1958; Rowe and Cleary, 1960). Some of these infants may be cured, if they are subjected to operation before irreversible changes have occurred, especially if they suffer from patent ductus arteriosus with pulmonary hypertension (Gammelgaard and Therkelsen, 1957; Jacobsen and Skall-Jensen, 1959). Palliative operations may improve others, so that they will later be able to stand more radical surgical measures (Collins et al., 1959). Finally, the proper diagnosis is of value in the medical treatment of the patients and in the prognosis, including the decision whether or not they may later

be subjected to surgical measures; the latter applies, for example, in the presence of large atrial septal defects.

The fact that cardiac catheterisation and angiocardiology may also be performed with great advantage in this age group (Ziegler, 1954; Boesen et al., 1956; Fink et al., 1958; Lind et al., 1960) has improved the diagnostic possibilities.

The purpose of this study is to report the experience gained in a series of consecutive cases and, particularly, to clarify the diagnostic value of cardiac catheterisation and selective cine-angiocardiology.

Clinical Material

The series consists of all patients under 2 years of age who during the four-year period 1956-1959 were referred to the Paediatric Clinic of the University Hospital, Aarhus, with suspected con-

Table 1. Survey of the series.

Result of examination for heart disease	Not subjected to cardiac catheterisation	Subjected to cardiac catheterisation	Total
No heart disease.....	30	1	31 (15 %)
Diagnosis uncertain; to return for later examination.....	13	0	13 (7 %)
Unquestionable congenital heart disease..	59	98	157 (78 %)
Total.....	102	99	201
Male.....	48	48	96 (48 %)
Female.....	54	51	105 (52 %)

Table 2.

Age distribution.

Age, in months	No heart disease	Diagnosis uncertain; to return for later examination	Congenital heart disease; no heart catheterisation	Congenital heart disease; catheterised	Total
0-2.....	7	6	26	16	55
3-6.....	7	1	17	19	44
7-12.....	6	5	8	29	48
13-24.....	11	1	8	34	54

genital heart disease, viz. a total of 201. A survey is given in Table 1. Clinical examination, electrocardiography and radiography – and in one case, cardiac catheterisation – revealed that congeni-

Table 3.

Cause of admission to hospital for heart disease.

	No heart disease	Congenital heart disease	Total
Symptoms.....	10	86	96 (51%)
Murmur.....	15	63	78 (42%)
Other signs.....	6	4	10 (5%)
Not admitted for heart disease (autopsy finding).....	0	4	4 (2%)

tal heart disease was absent in 31 patients (15%), while it could not be determined with certainty whether organic heart disease was present in 13 cases (7%). Owing to the good general condition of these patients, it was decided that they should return later for final diagnosis; this second group is excluded in the following account. Unquestionable congenital heart disease was revealed in a total of 157 cases (78%), including 98 in which catheterisation was performed. The experience gained in cardiac catheterisation in the 99 patients, if necessary supplemented by

angiocardiology, is analysed in detail below. The group of 59 patients with unquestionable heart disease who were not catheterised consisted partly of very poor children who died before they were brought into a condition allowing special investigations, and partly of children whose clinical condition was so good that cardiac catheterisation could be postponed, without harm, until the age of 3 or 4 years, when it can be performed without general anaesthesia. However, a few patients of the latter category are also included in the catheterised group, because we paid regard to the parents' wish to have the outlook determined as soon as possible. This explains why one normal individual has been included in the catheterised group.

The ages of the children at the time of examination appear from Table 2; 27 % were under 2 months and 72 %

Table 4.

Aetiology, etc.

	No heart disease	Congenital heart disease
Known cases in the family . .	0	8 (5%)
German measles in the mother during pregnancy.....	0	5 (3%)
Extracardiac anomalies.....	1	31 (26%)
Premature delivery.....	1	25 (16%)

Table 5. Body weight.

	No heart disease	Congenital heart disease
Normal body weight.....	21	35
More than 10% underweight.	8	55
More than 25% underweight.	2	63
No weight available (very sick patients).....	0	4

under 12 months. Cardiac catheterisation was not performed in a relatively large number of the youngest infants, because this group contained some of those who were so poor that they died before this investigation could be made.

Table 3 shows the symptoms and signs which occasioned that the children were admitted for investigation for congenital heart disease. It is seen that one half of the patients were referred to the hospital because of several symptoms, while cardiac murmurs had been observed in 42%; a few were referred to us for other reasons, for example, because routine radiography had revealed signs of cardiac disease.

The series does not give much information as to the aetiology of congenital heart disease (Table 4). In 5% of the patients, familial occurrence of similar cases was known, while information of rubella during the first trimester of pregnancy was available in about 3%. These percentages are minimum figures, since only absolutely unquestionable cases are included.

It is well known that many infants with congenital anomalies are premature. In our series, the birth weight had been below 2500 g in 16% of the patients with heart disease, but only

in one case among the 31 infants without such disease.

The frequency of extracardial anomalies is also shown in Table 4. Not less than about 25% of the children with cardiac disease had severe extracardial anomalies, such as harelip, cleft palate, mongolism, Klippel-Feil's syndrome, etc. This percentage is also a minimum figure, since minor defects, such as facial asymmetry, malformations of the external ear, etc., were not recorded, and internal anomalies, for example, in the urinary tract, may have been present.

Congenital heart disease is one of the serious diseases of infancy in which failure to thrive is a conspicuous symptom. In our series (Table 5), severe underweight was encountered in 40% of the children with cardiac disease as against only 6% of those without heart disease, and normal body weight was seen in only 22% of the former as compared with 68% of the latter. That this symptom was not even more conspicuous was due to the fact that several of the children were so young that failure to thrive had not yet manifested itself by an abnormally low body weight at the time of examination. If the birth weight is normal, it often takes more than 2 months before the body weight is reduced to less than 75% of normal. However, our series confirms the value of this symptom, which must be considered to be so important that failure to thrive which cannot otherwise be definitely explained constitutes an indication for investigations for congenital heart disease.

Clinical Data

The most important data in the various types of anomalies revealed in the 99 patients in whom cardiac catheterisation was attempted are shown in Table 6. The purpose of this tabulation is to characterise the series and to give the background to the use of cardiac catheterisation and angiocardiology. We do not intend to survey the possibilities of making a diagnosis by clinical examination, electrocardiography and radiography alone. It will often be possible to make a tentative diagnosis, although

this is rarely as reliable as in older children.

Only a few electrocardiographic and radiographic findings are listed in the table, especially those which are only to a slight extent affected by technical difficulties in the examination of small children, who are often restless and in a poor clinical condition. In particular, as far as radiography is concerned, it is our experience that only in exceptional cases in this age group does a more detailed analysis of the chambers, vascular trunks and pulsatory conditions

Table 6. Clinico-roentgenological findings.

	Sex		History				
	Male	Female	Cyanosis	Dyspnoea	General weakness	Recurrent respiratory tract infections	No symptom
Congenital heart disease, uncertain type . .	1	2	0	3	1	0	0
Isolated pulmonary stenosis	1	1	0	1	0	1	0
Ductus arteriosus persistens	2	9	0	3	1	9	2
Aortico-pulmonary fistula	0	1	1	0	0	0	0
Ventricular septal defect	10	8	2	12	3	10	2
Atrial septal defect	5	3	1	3	4	7	1
Ebstein's anomaly of the tricuspid valve . .	1	0	1	1	1	0	0
Ventricular septal defect and ductus arteriosus persistens	1	2	1	3	1	1	0
Pulmonary stenosis and ventricular septal defect	4	0	2	1	1	2	0
Other combined anomalies without cyanosis	2	1	1	2	0	0	1
Tetralogy of Steno-Fallot	7	15	19	16	14	8	2
Morgagni's syndrome	0	1	1	1	0	0	0
Tricuspid atresia with other anomalies . . .	3	1	4	3	2	0	0
Transposition of the great vessels	6	2 ^{b)}	6	7	2	1	1 ¹⁾
Truncus arteriosus persistens	0	1	0	0	1	0	0
Cor univentriculare	2	2	2	1	2	2	0
Dextrocardia and allied cases	2	1	3	3	0	2	0
Tumor cordis	0	1	0	1	0	1	0
Normal heart	1	0	1	1	0	0	0
Total	48	51	45	62	33	44	9

¹⁾ In 3 cases the heart volume could not be measured.

²⁾ One of the cases was a "corrected" transposition.

give so unquestionable information that this is of real diagnostic value. The high frequency of enlargement of the thymus adds to the difficulties encountered in the estimation of the vascular trunk. By enlargement of the heart (Table 6) is understood a heart volume of at least the predicted volume plus 3 times the standard deviation. The predicted figures and the standard deviation are those published by *Lind* (1950).

Table 6 requires only a few comments. Recurrent respiratory-tract infections are a characteristic symptom

in diseases with arteriovenous shunts (patent ductus arteriosus, atrial and ventricular septal defects), but are also frequently seen in diseases with low pulmonary blood flow (tetralogy of Steno-Fallot). The most remarkable feature in cardiac auscultation is that the typical murmur of a patent ductus arteriosus may very often be heard in this young age group (in seven of nine cases). Only rarely is it a completely continuous murmur; usually it continues from the systole into the diastole with a maximum about the second heart

Clinico-roentgenological findings.

No symptom	Clinical findings						Ecg.		Radiography				Total
	Cyanosis	Pre-cordial bulging	Faint systolic murmur	Loud systolic murmur	Diastolic murmur	Continuous murmur	Pro-nounced right axis deviation	Pro-nounced left axis deviation	In-creased heart volume ($\geq 3 \times \sigma$)	Normal heart volume	In-creased hilar vascular markings	De-creased hilar vascular markings	
0	1	1	1	2	1	0	1	0	2	1	1	2	3
0	1	0	0	2	0	0	1	0	1	1	0	0	2
2	0	6	0	4	3	7	1	1	10	1	10	0	11
0	0	1	1	0	0	0	0	0	1	0	1	0	1
2	2	11	1	17	3	0	3	0	13	5	16	0	18
1	0	1	0	8	2	0	2	0	5	3	4	0	8
0	1	1	0	1	0	0	0	0	1	0	0	1	1
0	2	2	0	2	0	1	0	0	3	0	3	0	3
0	0	2	0	4	1	0	2	0	2	2	2	1	4
1	0	2	1	1	0	1	1	1	2	1	3	0	3
2	21	1	4	17	1	1	18	0	4	17 ¹⁾	0	21	22
0	1	0	1	0	0	0	1	0	1	0	0	1	1
0	4	0	2	2	0	0	0	3	1	3	0	3	4
1 ¹⁾	7 ²⁾	5	2	5	0	0	7	0	7	0 ¹⁾	7	0	8
0	0	1	0	1	1	0	0	0	1	0	1	0	1
0	2	3	0	4	1	0	1	0	2	1 ¹⁾	2	2	4
0	3	0	0	1	0	1	—	—	2	1	0	1	3
0	0	1	0	0	0	0	1	0	1	0	0	0	1
0	0	0	1	0	0	0	0	0	0	1	0	1	1
9	45	38	14	71	13	11	39	5	59	37 ¹⁾	50	33	99

sound, and some experience is required to recognise the typical character of the murmur in the presence of the rapid heart action. Other authors have reported an essentially lower frequency of this typical ductus murmur (see, e.g., *Boesen, 1957*). Precordial bulging is a very reliable sign of cardiac enlargement. Only in two out of 38 patients with precordial bulging did radiography reveal a heart of normal size. On the other hand, the reverse does not apply: cardiac enlargement may very well be present without accompanying bulging of the precordium.

Cardiac Catheterisation and Angiocardiography

Cardiac catheterisation was attempted in 99 and accomplished in 96 patients. In one case, the procedure was abandoned because of cardiac arrest during the induction of anaesthesia (see below); in two others, it was abandoned because of too narrow veins. Angiocardiography was performed in 44 of the 96 patients.

Technique of Examination

Anaesthesia. — While we use only premedication with phenobarbital and local anaesthesia in older children and adults, general anaesthesia is employed in children under 2 years of age. As our investigations take relatively long time, a combination of rectal anaesthesia and inhalational anaesthesia with nitrous oxide, oxygen and ether is used, and nearly all the patients are intubated. In addition, we apply local anaesthesia to the site of venesection, so that the patients need only be lightly anaesthetised.

With a view to the blood analyses, the oxygen percentage in the inspiratory air is kept at a constant level during the diagnostic work, usually at about 30 %.

The anaesthesia was of fairly long duration.

The catheterisation itself took less than 1 hour in nine, between 1 and 2 hours in 40, and more than 2 hours in 47 patients, including the time for angiocardiography, when this was performed. The examinations are thus largely of longer duration in small children than in older ones and in adults.

The strenuous anaesthetics in poor children obviously enhance the risk involved in the investigations. Serious complications referable to the anaesthesia were encountered in two cases, one of which terminated fatally. The patients concerned were:

1. *A boy, aged 14 months.* — Before catheterisation, the tentative diagnosis was one of pulmonary stenosis, possibly associated with an atrial septal defect. Shortly after the intubation, pronounced bradycardia and respiratory depression occurred. Manual ventilation was soon followed by complete cardiac arrest (electrocardiographic control). Thoracotomy was performed at once, and the heart was re-started by cardiac massage. Signs of depressed cerebral function (respiratory arrest, absence of reflexes, stiff, dilated pupils) persisted for some time, but complete restitution occurred after 4 hours.

2. *A girl, aged 4 months.* — The diagnosis was one of corrected vascular transposition. Difficulties were encountered during intubation; the tracheal tube entered the right main bronchus and occluded the left (oxygen saturation in the left pulmonary vein 65 %), during which periods of severe bradycardia occurred. However, after withdrawal of the tube, catheterisation and angiocardiography proceeded smoothly, but after the examination atelectasis of the left lung developed, accompanied by respiratory distress with stridor and abundant secretion. The patient succumbed in a hypoxic attack 14 hours after the examination. Autopsy showed that death was due to obstruction of the respiratory tract caused by swelling of the tracheal and bronchial mucosae and tough secretion.

In the remaining patients, complications and sequelae of the anaesthesia could not be differentiated from those referable to the investigations as a whole. These complications are described below.

Blood loss. — The blood group of the patient is determined before catheterisation, and immediately after the introduction of the catheter a compatibility test is performed with the donor blood which is kept ready during angiocardiography.

In these young patients, the blood loss, including the amount of blood withdrawn as blood samples, must be closely controlled. The number of blood samples must be adjusted to the diagnostic problems. We took more than 10 blood samples in 50 of the 96 catheterisations accomplished. Also in this age group there is a tendency towards a larger number of blood samples in order to be able to calculate the relative shunts with a greater accuracy. For example, the average blood loss per examination in 1957 was 25 ml. Only in the cases in which the blood loss was unusually large as compared with the body weight was it replaced by transfusion through the catheter.

Obviously, the amounts of fluids administered must also be controlled. In this connexion, it is a great advantage that the Danish stopcocks for catheters and manometers are so tight that continuous infusion through the catheter is not required; occasional flushing of the catheter with a little heparin saline will suffice.

Methods of analysis. — The peripheral blood pressure (cuff method) and the rectal temperature are followed by the anaesthetist.

The intracardial pressures are recorded by the *Tybjerg Hansen* manometer (1949). The blood samples are analysed by Brinkmann's haemoreflexor (*Zijlstra*, 1958), in which only 0.5–1.0 ml blood is required for each analysis. The analyses are performed during the catheterisation, so that further supplementary blood samples may be withdrawn, if necessary.

The intracardial pressures and the electrocardiograms are followed visually on a cathode-ray oscilloscope; in addition, the electrocardiogram is followed by an auditory signal, the pitch of which is modulated by the waves of the electrocardiogram.

Technique of cardiac catheterisation. — In this age group, it is usually best to use the great saphenous vein, since the arm veins are usually too narrow. Only if the diagnostic problem is to determine the type of an isolated atrial septal defect, which is, however, necessary only in exceptional cases in young infants, should it be attempted to use a vein of the arm. In small infants, even the great saphenous vein may be too narrow. We have not used the femoral vein because this involves a certain amount of risk. The distribution in our series is as follows: —

Cardiac arrest during anaesthesia, catheterisation abandoned	1
Catheterisation abandoned, great saphenous vein too narrow ..	2
Cubital cephalic vein used	3
Great saphenous vein used	93
	99

Thus, catheterisation was accomplished in 96 of 99 cases. The effectiveness of the investigation depends to a great extent on the size of the catheter which can be inserted. A catheter No. 4 renders both the investigation itself and the blood sampling difficult and often results in slightly damped pressure curves and, owing to the low rate of injection, in a less successful angiocardiology. In this age group, catheter No. 5 or, still better, No. 6 or even a larger one gives a possibility of optimal results of catheterisation and angiocardiology. In nine of our 96 patients, the vein was so narrow that only catheter No. 4 could be introduced. In seven of these nine patients it was nevertheless possible to determine the main type of the cardiac anomaly, which shows that a fairly correct diagnosis may be obtained even in the presence of very narrow veins.

Technique of angiocardiology. — So far, we have been hampered in our work in this field by the fact that the equipment for angiocardiology was available only in the Radiological Clinic situated in another wing of the hospital. Accordingly, when we wished to conclude the study with angiocardiology, we had to carry the anaesthetised and intubated patient about 200 metres through a cellar tunnel to that clinic. This has caused that we, in a few cases in which angiocardiology was otherwise desirable, omitted this part of the examination for reasons of safety.

Before the transport of the patient to the Radiological Clinic we injected a test dose of the contrast medium through the catheter. None of the patients in this series showed allergic reactions in the form of blood-pressure fall or skin rash.

Apart from the first cases in the series, we have invariably used Urografin 76 %, injected in an amount of 1.0–1.5 ml per kg body weight. Of the 44 patients subjected to angiocardiology, 20 received more than one injection. The injections did not cause any undesirable symptoms.

Now we always change the catheter before angiocardiology, using a catheter with a closed tip and four side holes near the tip, but this type has become available so late that it has been used only in the last nine cases. In the other cases, a Lehmann catheter was used.

In the majority of the cases, the contrast medium was injected under manual pressure by means of a syringe mounted on a stand provided with a long lever. This gives a relatively high, but uncontrollable rate of injection. In the more recent cases, *Gidlund's* high-pressure syringe (1956) was used.

Apart from the first two cases, in which an Odelca camera with a rapidix cassette was employed, we used a 5 in. image amplifier (Philips) with cinematography (Arriflex camera) in one plane with 35 mm film and 48 exposures per second under fluoroscopic control. When necessary, we used exposures in several planes, with repeated injections of contrast medium as stated above. The results

of the catheterisation served as a guide in the choice of the site of injection and the projections ("selective angiocardiology").

The exposures were interpreted by means of a viewing equipment with a picture rate variable within the range of 0-50 frames per second.

Results

The types of congenital cardiac disease in our patients appear from Table 7. The multiplicity of types is very great in this age group and is actually greater than shown in the table, since the variation with regard to details is considerable in some of these anomalies, especially in transposition of the great vessels, single ventricle and dextrocar-

Table 7.

Types of anomalies in the patients with congenital heart disease (*in vivo* diagnoses, supplemented by autopsy findings).

	Not catheterised	Catheterised	Total
Coarctation of the aorta.....	3	0	3
Isolated pulmonary stenosis.....	0	2	2
Ductus arteriosus persists.....	3	11	14
Aortico-pulmonary fistula.....	0	1	1
Ventricular septal defect.....	4	18	22
Atrial septal defect.....	1	8	9
Ebstein's anomaly of the tricuspid valve.....	0	1	1
Cor triatriatum.....	1	0	1
Ventric. septal defect and ductus art. persists.....	0	3	3
Pulmonary stenosis and ventricular septal defect.....	0	4	4
Other combined anomalies without cyanosis.....	1	3	4
Tetralogy of Steno-Fallot.....	1	22	23
Morgagni's syndrome.....	0	1	1
Tricuspid atresia with other anomalies.....	2	4	6
Transposition of the great vessels.....	3	8	11
Truncus arteriosus persists.....	0	1	1
Cor univentriculare.....	0	4	4
Dextrocardia and allied cases.....	3	3	6
Fibroelastosis without other anomalies.....	4	0	4
Tumor cordis.....	0	1	1
Disturbances of rhythm without other anomalies.....	2	0	2
Congenital heart disease of uncertain type.....	31	3	34
Total.....	59	98	157

Table 8.

Survey of principal diagnostic results.

	Total	Angio- cardio- graphy per- formed	Information obtained by angiocardiology			Over-all result			
			Deci- sive	Sup- ple- men- tary	Insig- nifi- cant	De- tailed diag- nosis	Certain details mis- sing	Diag- nosis uncer- tain	Diag- nostic errors
Cardiac catheterisation failed	3	—	—	—	—	—	—	3	—
Cases not clarified at catheterisation..	19	17	12	2	3	12	1	4	2
Main type of anomaly clarified at catheterisation	20	14	6	8	—	12	8	—	—
Cases fully clarified at catheterisation	57	13	—	11	2	57	—	—	—
Total	99	44	18	21	5	81	9	7	2

dia. In addition to clinical examination, electrocardiography and radiography, the diagnoses in Table 7 are based on findings revealed in cardiac catheterisation, angiocardiology, operation and autopsy.

Obviously, special interest attaches to the *in vivo* diagnoses in the patients who did not undergo operation and to the pre-operative diagnoses in those afterwards subjected to operation. In these young patients, the past history is generally of little importance in the diagnosis; some more information may be obtained, although usually less than in older children, by the clinical examination, electrocardiography and radiography but cardiac catheterisation will nearly always, and angiocardiology often, be necessary to make an accurate diagnosis.

The results obtained in cardiac catheterisation and angiocardiology in the present series are reported below.

The principal results are shown in Table 8. By the expression "main type of anomaly clarified" is understood that cardiac catheterisation clarified the principal type of the anomaly, although certain details were missing, for example,

the type of the pulmonary stenosis in the tetralogy of Steno-Fallot, or the exact anatomical conditions of the pulmonary artery in transposition of the great vessels and tricuspid atresia. The other groups are self-explanatory.

It is seen from Table 8 that cardiac catheterisation gave an accurate diagnosis in more than one half of the patients (in 57 of 96 cases), while the main type of the anomaly could be determined in three quarters of the patients (in 77 out of 96 cases).

Supplementary angiocardiology was performed in 44 patients including 13 in a good clinical condition in whom the anomaly had been fully clarified by catheterisation; the latter group was studied in order to gain experience. Angiocardiology gave decisive information in 18 of the remaining 31 patients in whom this investigation was fully justified, viz. in 12 in whom the details had not been fully clarified and in six in whom only the type of the anomaly had been determined by catheterisation.

The over-all result of the special diagnostic investigations in the 99 patients may be summarised as follows: —

Table 9.

Diagnostic result of cardiac catheterisation.

	Exami- nation failed	Uncer- tain diagnosis	Main type determined	Accu- rate diagnosis	Total
Isolated pulmonary stenosis.....	—	—	—	2	2
Ductus arteriosus persistens.....	—	—	—	11	11
Aortico-pulmonary fistula.....	—	—	1	—	1
Ventricular septal defect.....	1	—	2	15	18
Atrial septal defect.....	—	—	—	8	8
Ebstein's anomaly.....	—	—	—	1	1
Combined anomalies without cyanosis.....	—	1	3	6	10
Tetralogy of Steno-Fallot.....	—	7	5	10	22
Morgagni's syndrome.....	—	1 ¹⁾	—	—	1
Tricuspid atresia with other anomalies.....	—	1	3	—	4
Transposition of the great vessels.....	—	2	5	1	8
Truncus arteriosus persistens.....	—	1	—	—	1
Cor univentriculare.....	—	1	1	2	4
Dextrocardia and allied cases.....	—	3	—	—	3
Tumor cordis.....	—	1 ¹⁾	—	—	1
Uncertain diagnosis.....	2	1	—	—	3
No heart disease.....	—	—	—	1	1
Total.....	3	19	20	57	99

¹⁾ Diagnostic errors, see the text.

1. A detailed *in vivo* diagnosis was obtained in 81 cases.

2. The principal type of the anomaly was clarified, but certain details were missing in nine cases. — This group consisted of one patient with tricuspid atresia, one with a large ventricular septal defect, one with large atrial and ventricular septal defects, one with a univentricular heart, and five with transposition of the great vessels.

3. The diagnosis of the type of the anomaly was uncertain in seven cases. — In addition to the three patients in whom cardiac catheterisation could not be accomplished, this group comprised one case of complicated dextrocardia, one with a univentricular heart, one with transposition of the great vessels, and one with pulmonary hypertension,

possibly as a complication of fibro-elastosis.

4. The diagnosis was erroneous in two cases. — In one patient with atrial septal defect and pulmonary stenosis (Morgagni's syndrome), the anomaly was diagnosed as the tetralogy of Steno-Fallot. The second patient had a cardiac tumour, a large teratoma mainly arising from the anterior aspect of the right atrium, while our diagnosis was one of atrial septal defect, possibly with certain complications, which we found would not contra-indicate operative closure of the defect. Operation revealed an atrial septal defect of only minor importance. That the tumour had passed unrecognised was due to the fact that angiocardiology had been performed only in one plane.

Cardiac catheterisation with angiography thus resulted in a detailed diagnosis in 82 % (81 of 99 patients) and revealed the main type of the anomaly in 91 % (90 of 99 patients).

Special Conditions Related to Cardiac Catheterisation

Diagnostically, cardiac catheterisation should actually be expected to be just as efficient in infants as in older children, but as it in our series – just as has previously been seen in others – resulted in a smaller percentage of detailed diagnoses, it is of interest to analyse the value of the method in the various types of anomalies. It is seen from Table 9 that the diseases in which it is very difficult to secure an accurate diagnosis by cardiac catheterisation alone are chiefly those that have so poor a prognosis that the patients usually die within the first two years of life, for example, the group of tricuspid atresia, transposition of the great vessels and univentricular heart. This lends support to our general impression that, except in the tetralogy of Steno-Fallot cardiac catheterisation is just as efficient in the diagnosis of congenital heart disease in patients under 2 years as in the older age groups. In the tetralogy of Steno-Fallot the pulmonary conus or the pulmonary ostium is narrower as compared with the diameter of the catheter than in adults, which makes it very difficult to introduce the catheter into the pulmonary artery in these young patients, in particular, if the catheterisation is performed through the great saphenous vein.

In addition to this special point, car-

diac catheterisation in very young children involves certain problems and possibilities which are briefly discussed below.

Owing to the pronounced respiratory fluctuation in the pressure, accurate calculation of the intracardial pressures is difficult, especially at low pressure levels.

Catheterisation of the right ventricle may be difficult when the catheter is introduced from the great saphenous vein. However, when some experience has been gained, it can nearly always be accomplished. In our series, the right ventricle was not catheterised in five patients. In four of these, the right ventricle was underdeveloped, and tricuspid atresia was present. It must therefore be concluded that when it is impossible to catheterise the right ventricle, this provides strong evidence in favour of a diagnosis of atresia or stenosis of the tricuspid ostium.

Right ventricular pressures are summarised in Table 10. When, as was done in this series, cardiac catheterisation is used only in exceptional cases in this age group if the patients are not affected by their heart disease, an unstrained right ventricle will rarely be encountered; not less than 82 of 91 patients revealed an increased pressure. In the majority of these 82, viz. 57 cases, the increase was so pronounced that the pressures in the two ventricles were equalised. Equalisation of pressures is also a constant finding in the older age groups in the presence of certain types of anomalies and simply a consequence of the wide communications, for example, in the tetralogy of Steno-Fallot (Götzsche et al., 1952) and

Table 10.

Right ventricular systolic pressure.

	Close to the systolic blood pressure	Increased but lower than the systolic blood pressure	Normal
Isolated pulmonary stenosis.....	—	2	—
Ductus arteriosus persistens.....	4	7	—
Ventricular septal defect.....	8	5	4
Atrial septal defect.....	1	4	3
Other cases without cyanosis.....	8	4	1
Tetralogy of Steno-Fallot.....	21	—	—
Morgagni's syndrome.....	1	—	—
Cor univentriculare.....	4	—	—
Transposition of the great vessels.....	8	—	—
Truncus arteriosus persistens.....	1	—	—
Dextrocardia and allied cases.....	1	2	—
Normal individual.....	—	—	1
Uncertain diagnosis.....	—	1	—
Total.....	57	25	9

univentricular heart, while in other anomalies it is a striking feature that they are often associated with malignant pulmonary hypertension. The latter observation is made, for example, in ventricular septal defect and patent ductus arteriosus.

Direct catheterisation of the aorta from the right ventricle should be endeavoured, if this is supposed to be possible in view of the anatomical conditions. This gives good information as to the presence or absence of shunts and accurate information as to the origin of the aorta from the heart. The relations of the aortic arch is revealed by this examination, whereas contrast filling is usually required for the clarification of the origin of the great branches from the aorta. As is always the case in cardiac catheterisation, it is therefore here of great importance that the course of the catheter is closely studied in all projections. Of the 91 patients in whom the right ventricle could be catheterised,

61 had diseases of such a nature that it should theoretically be possible to catheterise the aorta from the right ventricle, and this catheterisation was actually performed in 36. Further details appear from Table 11. It is seen that, in practice, catheterisation of the aorta can always be performed in the presence of transposition of the great vessels, often in univentricular heart, but only in about one half of the cases of ventricular septal defect and tetralogy of Steno-Fallot.

For purely anatomical reasons, *catheterisation of the pulmonary artery* is often difficult or impossible in the presence of certain anomalies which occur either chiefly or exclusively in children under 2 years of age. Among the 91 patients in whom the right ventricle could be catheterised, catheterisation of the pulmonary artery proved impossible in 25. The diagnoses in these 25 cases are listed in Table 12. The difficulty in catheterising the pulmonary artery is

a specific feature in this age group and its diseases. In older children it is nearly always possible.

An atrial septal defect or a patent foramen ovale could be catheterised in 49 of the 50 patients of whom it is known that they had such a defect. The case in which the catheter could not be passed was one of the few in which only an arm vein was used, and the foramen ovale was very small and functionally closed. From this the conclusion can be drawn that an interatrial communication can be ruled out if the catheter cannot be passed through when catheterisation is performed from the leg. It may be mentioned that our previous experience has shown that in catheterisation from an arm vein a small foramen ovale may easily be overlooked. On the other hand, the evaluation of the type of an atrial septal de-

fect with a view to method of operation – primum or secundum defect – is very difficult in catheterisation from the leg.

An interatrial communication is thus very frequent in congenital heart disease in this age group, which is often an advantage, since it renders it possible to perform angiocardiology with injection of contrast medium into the left side of the heart.

In our experience, *catheterisation of a patent ductus arteriosus from the pulmonary artery* is facilitated when the catheter is introduced from the leg. In the present series, the catheter could be passed through the patent ductus in all cases in which this was the main anomaly.

Other data which can be obtained by cardiac catheterisation are not considered in detail here, but the method is helpful in the demonstration of shunts and estimation of their size, in the "palpatory" estimation of chambers, defects and vessels, including the direct demonstration of venous anomalies, and in the evaluation of valvular defects other than pulmonary stenosis. It is

Table 11.

Catheterisation of the aorta.

	Right ven- tricle cath- eterised	Aorta cath- eterised from the right ven- tricle
Tetralogy of Steno-Fallot.....	21	12
Ventricular septal defect.....	17	8
Cor univentriculare.....	4	3
Transposition of the great vessels.	7	7
Corrected transposition of the great vessels.....	1	0
Truncus arteriosus persistens....	1	0
Dextrocardia and allied cases....	3	1
Ventric. septal defect + pulmonary stenosis.....	4	3
Ventric. septal defect + ductus art. persistens.....	2	1
Ventric. septal defect + atrial sep- tal defect.....	1	1
Total.....	61	36

Table 12.

Catheterisation of the pulmonary artery.

	Right ven- tricle cath- eterised	Pul- monary artery not cath- eterised
Tetralogy of Steno-Fallot.....	21	9
Transposition of the great vessels.	8	8
Cor univentriculare.....	4	2
Morgagni's syndrome.....	1	1
Dextrocardia and allied cases....	3	2
Combined cases without cyanosis.	7	3
Other anomalies.....	47	0
Total.....	91	25

our experience that cardiac catheterisation may here give just as complete information within these fields as in other age groups, apart from the fact that shunt calculations are only relative, since the oxygen uptake cannot be measured.

Special Conditions Related to Angiocardiography

A small amount of contrast medium was in this series always injected as a test for allergy, and during this procedure we always took a radiograph in order to visualise some anatomical details. This resulted in a final diagnosis in three patients, so that further angiocardiography was unnecessary.

In 31 of 44 cases, angiocardiography was indicated for diagnostic reasons. In addition to the 44 cases which were actually studied, angiocardiography was indicated in another six cases, but was omitted for various reasons, for example, poor clinical condition. Thus, among the 96 patients in this age group in whom cardiac catheterisation was accomplished, angiocardiography was indicated in 37 (i. e. $31 + 6$) cases or about 40 %, when the necessity of this examination was adjudged from a diagnostic point of view.

The principal diagnostic results obtained by angiocardiography in this series has already been mentioned. Here we shall consider a few special points in order to throw light on the value of the cine-angiocardiographic method.

The tetralogy of Steno-Fallot is the group of diseases in which most angiocardiographies were performed, viz. in 17 cases. The injection was given into

the right ventricle in 16 and into the inferior vena cava in one. The filling of the aorta from the right ventricle could be seen in all 17 patients. On the other hand, the pulmonary artery was sometimes poorly visualised because of a low pulmonary blood flow, insufficient image sharpness in cinematography, and – when only one projection was used – because of overshadowing by other structures. The type of the pulmonary stenosis was determined by angiocardiography in 12 of the 17 patients, but in five of these it had already been revealed by cardiac catheterisation, and in one of the remaining autopsied cases the estimate was wrong. On the other hand, cine-angiocardiography gives an excellent impression of the pulmonary blood flow in relation to the veno-arterial shunt from the right ventricle to the aorta.

Tricuspid atresia with hypoplasia of the right ventricle was revealed in four patients in whom angiocardiography was performed with injection, inter alia, into the left half of the heart. In all four cases, cine-angiocardiography clarified the functional conditions, especially the relation between the blood flow through the aorta and the pulmonary artery, but in three of the patients the anatomical details as regards the origin of one of the vessels from the communicating ventricles were uncertain (Fig. 1).

In one of the four patients with *transposition of the great vessels* subjected to angiocardiography, the examination was unsuccessful (catheter No. 4, poor contrast filling). In two of the patients we did not obtain details as regards the origin of the pulmonary ar-



FIG. 1.—Tricuspid atresia; left anterior oblique position. Both great vessels arise from the left ventricle. The origin of the pulmonary artery is not clearly visualised.

tery from the heart, while the transposition of the aorta was clearly visible, but this was known from the catheterisation. However, the injection of contrast medium was performed into the left atrium. In the light of our later experience, it is beyond doubt that when this anomaly is suspected, the contrast medium should be injected into the left ventricle, which will usually be possible by catheterisation through an atrial septal defect. This was done in the fourth case, in which the anatomical conditions were completely clarified by angiocardiology.

Of the two cases of *dextrocardia* and one of *situs inversus* with *laevocardia*, all with complex anomalies, angiocardiology clarified the anomaly in two cases. Here the flow relations were also clearly seen, but anatomical details of the pulmonary ostium were lacking.

Angiocardiology was performed in three patients with *atrial septal defect*, all with injection into the left atrium. The diagnosis had been made by cardiac

catheterisation; angiocardiology confirmed this diagnosis, but did not give information as to the type of the defect (*primum* or *secundum*, etc.).

Two patients had an isolated *ventricular septal defect*. In both patients, the catheter was passed into the left atrium through a non-functioning foramen ovale. In one of the cases, the contrast medium showed merely a shunting to the right side, while the site of the defect was not visualised. The second case is of special interest. Here, a small cloud of contrast medium was seen in two brief phases entering the outflow tract of the right ventricle from the left ventricle (Fig. 2). It was so brief that successful visualisation might be difficult in ordinary seriography, whereas it was distinctly seen in projection of the cinefilm. In this patient, cardiac catheterisation had revealed a small arteriovenous shunt to the right ventricle. From the observations made in this case it may be concluded that even in favourable cases (injection of the contrast medium into the left side of the heart, 48 exposures per second) angiocardiology does not reveal ventricular septal defects which are so small that an arteriovenous shunt cannot be demonstrated by cardiac catheterisation with a large number of blood samples.

Three patients subjected to angiocardiology were acyanotic with a combination of *pulmonary stenosis* and *ventricular septal defect* ("acyanotic Steno-Fallot"). In all three cases, the pulmonary stenosis and its type could be seen, while the ventricular septal defect disclosed by cardiac catheterisation could not at all be visualised. In such patients, angiocardiology is therefore

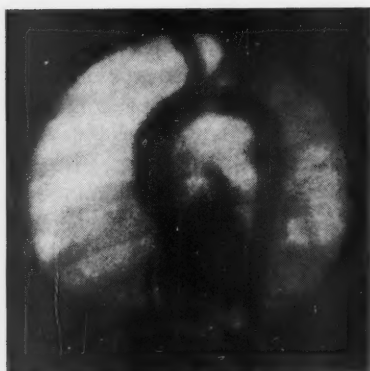


Fig. 2a.

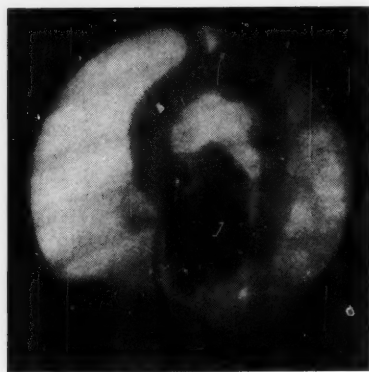


Fig. 2b.

FIG. 2.—Isolated ventricular septal defect; left anterior oblique position (a and b). A jet of contrast medium entering the right ventricle is seen only during the systole (b).

apparently indicated only when the pulmonary stenosis or its type has not been demonstrated by cardiac catheterisation.

The remaining eight patients in whom angiocardiology was performed had various anomalies. The study resulted in distinct visualisation of an aortico-pulmonary fistula (previously published, see *Skall-Jensen*, 1958) and a patent truncus arteriosus. The other six patients did not present any features of special interest.

Complications

The complications occurring in cardiac catheterisation with or without selective angiocardiology under anaesthesia in our series are shown in Table 13. Extrasystoles, sporadic or in series, are not included, since these are nearly constant phenomena in these examinations.

Two deaths occurred within one week after the examination. These patients were under 2 months of age, very ill prior to the cardiac catheterisation,

and had transposition of the great vessels. They went gradually downhill without any steep change in the condition after the examination. In view of this and our knowledge of the prognosis of transposition, these two deaths

Table 13. Complications.

	No. of cases
Sequelae of tracheal intubation terminating fatally.....	1
Cardiac arrest during induction of anaesthesia.....	1
Excessive bradycardia during intubation.....	1
Paroxysmal tachycardia of long duration.....	1
Atrio-ventricular block.....	2
Bundle-branch block.....	3
Sinus arrest with idioventricular rhythm.....	1
Haemorrhage.....	1
Transient venous congestion from ligation.....	1
Haematoma at the site of venesection.....	1
Total.....	13
	(in 12 patients)

are not included under the complications, although it cannot be ruled out with certainty that the fatal outcome may have been hastened by a few days.

With this reservation, the main result is thus that one death was directly referable to the examination as a complication of the anaesthesia. This gives a mortality of 1 %. Apart from the case with cardiac arrest, the other complications were slight, and of only a transient nature.

Discussion

In order to obtain unbiased information as to the differential diagnosis in congenital heart disease in infants we have analysed a series of 201 consecutive cases in which the patients were examined according to the present routine. This does not imply that the series is unselected. Extremely sick children, who would probably not tolerate an operation at the time of examination, are not catheterised; some of these children will die undiagnosed. Children without symptoms are not subjected to cardiac catheterisation within the first two years of life unless the parents want to obtain particulars concerning the prognosis and the chance of operability without delay. We prefer a less hazardous examination under local anaesthesia at the age of 4–5 years.

According to these principles, about one half of the children under 2 years of age who were referred to our hospital with suspected congenital heart disease were subjected to cardiac catheterisation. Supplementary selective angiocardiology was found to be indicated in about 40 % of the catheterised

cases, which is a definitely higher incidence than in older patients.

As a detailed description of consecutive cases in series of infants is unusual, we have presented some details observed in our patients, accompanied by a tabular survey of the clinical findings.

Most of the patients were referred to hospital within the first year of life – many even during the first months of life, mainly infants with very severe symptoms. Half of the children were referred to us because of symptoms, 85 % of the remaining cases being suspected of congenital heart disease because of a cardiac murmur. In this age group there is a remarkably high percentage of prematurity, viz. 15 %, and the incidence of concomitant extracardiac malformations is also very high, about 25 %. The corresponding figures in a series of congenital heart disease after the age of 2 years (Götzsche, 1952) were: prematurity, 8 %; extracardiac anomalies, 9 %. These features must then be closely related to severe cardiac anomalies. Another feature which is much more conspicuous in this age group than in older patients is the high incidence of pronounced underweight; 40 % of our patients weighed less than 75 % of the predicted body weight.

The clinical findings are briefly summarised in Table 6. It is our experience that only in exceptional cases can the diagnosis of the type of the cardiovascular anomaly be made with accuracy during life without cardiac catheterisation and/or angiocardiology. The outstanding exception is patent ductus arteriosus, in which we also found a typi-

cal murmur in most cases in this age group. One of the main reasons for the necessity of the special diagnostic procedures is that the characteristic radiographic findings in many anomalies, which have been so splendidly described by Taussig (1947) are actually not very common or easily demonstrable in these very small children.

Our experience with cardiac catheterisation in children under 2 years of age is based upon a series of 99 cases. The main conclusion is that catheterisation can be carried out with almost as good diagnostic results as in older children and adults, with the exception of the tetralogy of Steno-Fallot. The main type of cardiovascular anomaly was disclosed in about three quarters of all cases, whereas all details were revealed in only about one half of the cases. This is a definitely lower percentage than in older age groups, but a closer analysis shows that this is due to a higher incidence of anomalies which are less amenable to cardiac catheterisation alone (especially complicated cyanotic types).

As to the special problems of catheterisation techniques the main results are: The calculation of intracardiac pressures is often difficult because of very great respiratory oscillations. The inability to introduce the catheter into the right ventricle is closely related to tricuspid anomaly. The aorta can be catheterised through the right ventricle in about one half of the patients who are known to have a communication between the right ventricle and the aorta. Catheterisation of the pulmonary artery is extremely difficult in pulmonary stenosis in this age group. An in-

teratrial communication can always be passed by the catheter, when this is introduced into the heart through the great saphenous vein. A patent ductus can always be passed in cases where this is the principal anomaly.

During the period in question the angiocardigraphic method chosen was selective cine-angiocardigraphy. As in other contrast methods, the best diagnostic results are obtained in patients with veno-arterial shunts, whereas in arteriovenous shunts efficient visualisation is attained only in the presence of a co-existing interatrial communication allowing an injection to be made direct into the left side of the heart. Even under such ideal conditions, the accurate localisation of a defect may be doubtful.

Certain special features of *cine*-angiocardigraphy clearly disclose themselves in our series. The great fundamental *advantage* of the cine-technique is the high picture speed, partly allowing the registration of events taking place at a rapid rate, and partly making possible a repeated direct study of the flow through the various cavities and vessels. In practice, this means that smaller shunts and valve insufficiencies can be visualised by this method than by ordinary seriography, and that a fairly good estimate of the direction and relative magnitude of flows can be obtained, even if the anatomical details may be obscure. It may, for example, be clearly seen in slow motion whether a pulmonary artery in tricuspid atresia is filled from the ventricles or retrogradely from the aorta, even though the origin of the pulmonary artery is not distinctly visualised.

The greatest fundamental *disadvantage* of the cine-technique is the poor image sharpness. This means that, in particular, vessels and cavities with a diminished blood flow will be poorly defined and may easily be obscured by other structures. This is a serious objection to cine-angiocardiology, as most cases will be fairly well clarified by cardiac catheterisation except, perhaps, for some anatomical detail, which may be just what is obscured by the poor image definition in the cine-angiographic films. An important example of this is the type of pulmonary stenosis in the tetralogy of Steno-Fallot.

In our series, the combination of cardiac catheterisation and selective cine-angiocardiology resulted in a detailed diagnosis in 82 % of the patients, whereas the main type of the anomaly was disclosed in another 9 %; 7 % were obscure, and in 2 % there were diagnostic errors. These results are only slightly inferior to those obtained in older children, but the risk is definitely higher in young children, in whom general anaesthesia is required, as was mentioned in the section on complications.

Our main conclusions are, then, that cardiac catheterisation is also highly efficient in this age group, but should be undertaken only if reasonably indicated; that selective angiocardiology – preferably in two planes – is more

frequently indicated than in older age groups; and that cine-angiocardiology may be used for this purpose with fairly good results, but will be inferior to angiocardiology by ordinary serigraphic methods in many cases, and only superior in a few.

Summary

During the years 1956–1959 inclusive 201 children under 2 years of age were referred to hospital for investigation for congenital heart disease. In 31 cases, clinical and radiographic examination revealed normal conditions; in 13 cases, continued clinical observation was indicated. Congenital heart disease was revealed in 157. Of these, 59 were not subjected to cardiac catheterisation, either because they were in a very poor condition and died before the examination could be accomplished, or because their condition was so good that catheterisation, with advantage, could be postponed until the age of 3–4 years. Catheterisation was performed in 98, including 44 who were also subjected to angiocardiology. Of these 98 cases, 80 were fully clarified; the principal anomaly was disclosed in nine; the diagnosis was uncertain in seven (including three in whom catheterisation was unsuccessful); erroneous diagnoses were made in two. Death occurred in one case.

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PRELUXATION OF THE HIP JOINT

Diagnosis and Treatment in the Newborn
and

The Diagnosis of Congenital Dislocation of the Hip Joint
in Sweden during the Years 1948-1960

By

KURT PALMÉN

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ACTA PÆDIATRICA

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From the Pediatric Clinic,
Central Hospital, Falköping
(Chief: Dr Kurt Palmén)

PRELUXATION OF THE HIP JOINT

Diagnosis and treatment in the newborn
and

The diagnosis of congenital dislocation of the hip joint
in Sweden during the years 1948-1960

By

KURT PALMÉN

UPPSALA 1961

ALMQVIST & WIKSELLS BOKTRYCKERI AB

Translated by Maud Marsden

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*Affectionately dedicated to
my wife Ulla Palmén*

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TERMINOLOGY

Luxation of the hip joint = the femoral head has been completely displaced outside the acetabulum.

Dislocation = luxation.

Subluxation = a greater or lesser degree of displacement of the femoral head, without complete loss of contact with the acetabulum.

Preluxation = the state of readiness for dislocation which may be found in the new-

born, and which can be diagnosed by using Ortolani's abduction manoeuvre and by subluxation provocation. A greater or lesser degree of subluxation may already be present.

Dysplasia of the hip joint = the changes which may be observed on roentgen examination of cases of dislocation and subluxation, such as a sloping acetabulum (with a greater acetabular angle), and changes in the femoral head and neck.

HISTORICAL REVIEW

The history of congenital dislocation of the hip is the history of orthopedic surgery. This disease is the most common of the congenital skeletal deformities, and was described even in the oldest medical records. Some short historical data¹ will be given here as an introduction.

Hippocrates gave a typical description, and also stated that the disease could occur *in utero*. Ambroise Paré was the first to discover the hereditary nature of the disease (1678) and pointed out that the shallow acetabulum was an obstacle to reduction. As early as the end of the 18th century, Camper (1784) observed that the disease most often affected girls and had a greater frequency in certain districts; in a small Dutch village 125 persons were lame for this reason, a frequency of 3.6%.

The first exact pathologic and anatomic description of the autopsy finding was made by Paletta of Milan, in 1783 in a 15 day old boy with bilateral dislocation. In 1826 Dupuytren published an interesting treatise on dislocation of the hip, which he believed to be a new disease that he had discovered. Since he found, by anatomical examination, that the acetabulum was absent, he considered all treatment of this disease to be purposeless. Individual cases were, however, treated in Paris with long periods of extension, during the immediately following years, but without result (Jalade, Lafond, Humbert).

The first classical monograph on the different problems of dislocation was written in 1847 by Charles-Gabriel Pravaz, who as far as we know was the first person to suc-

ceed with a reduction. Pravaz used extension treatment lasting for 8–10 months, followed by daily attempts at reduction until he eventually succeeded, and the patient then lay flat for two years on a carriage. Not until then was a wheeled walking chair allowed. Pravaz pointed out also that the prognosis was better if the treatment was commenced early. His method met with some opposition, but was nevertheless used with good results in a number of cases. The age at the commencement of treatment was high throughout (4–12 years), which, of course, contributed to the bad results. Pravaz's method was used in England by Brodhurst (1866) and Adams (1888), and in the U.S.A. it was described in 1850 by Carnochan—the first case to be treated there does not appear to have been reported until 1885, by Brown of Boston.

In the German surgical congress of 1879, Roser postulated that dislocation of the hip was caused by an abnormal foetal position with greatly adducted legs, particularly in girls. He stated on this occasion: "Die frühzeitige Diagnose solcher Verrenkungen ist aber ganz gewiss die erste Bedingung ihrer Heilbarkeit. Ich glaube, dass viele dieser Fälle, sogar die meisten derselben, noch heilbar wären, wenn man die Krankheit an den Neugeborenen erkennen und wenn man dann sogleich die nötigen Abduktionsverbände anlegen würde."

During the years between 1880–1890, dislocations were also treated with different surgical methods in an attempt to improve the acetabular roof (Guérin, König, Poggi, Hoffa, Lorenz).

In 1888 Paci, a surgeon of Pisa, suggested that the method of reduction over the posterior acetabular edge, used for traumatic dislocations, should also be used for congeni-

¹ Mainly obtained from Valentin, *Geschichte der Orthopädie* (1960).

tal dislocation of the hip. A short time afterwards, in 1895, Adolf Lorenz of Vienna, on the basis of his experiences with open reduction, enunciated the modern principles of conservative treatment with manual reduction under anesthesia in one seance, subsequently attempting to retain the femoral head in a physiological position, where it is able to exert beneficial influence on the development of the acetabulum. Among thousands of newborn children, Lorenz found no dislocations. He suggested that this disease was an acquired deformity, arising from a congenital "anlage", an inhibitor of growth, especially of the acetabulum. He therefore introduced the term "die sogenannte angeborene Hüftverrenkung". Lorenz showed the advantages of his method in a long series of treated cases. By 1895 it had become possible to confirm the good primary results of treatment by roentgen examination.

Lorenz's method was quickly accepted, and it was then considered that this very old medical problem had reached its final solution.

It was later found, however, that even if the primary results of the treatment were good, the final results shown by follow-up examinations were less satisfactory.

Lorenz (1920) still considered in his monograph that the most favorable age for the commencement of treatment was after the child had begun to walk during its second year, and that reduction during the third year still gave almost as good results. He regarded a diagnosis before the child had begun to walk as rare and uncertain. He did not recommend any prophylactic treatment before obvious dislocation was manifest, and repudiated treatment during the first year of life, as suggested by various other surgeons (Bade 1907, Joachimsthal 1908 *inter alia*). Lorenz's principles were nevertheless still generally accepted. In spite of the fact

that he laid the foundation of the modern successful treatment of congenital dislocation of the hip, his dogmatic principles of postponing treatment at least until the child had begun to walk hindered for a long time the development of early treatment.

In Sweden also it was customary until the middle of the 1930's not to commence treatment before the age of 2-3 years. Even if the diagnosis was made earlier, the reduction was postponed until later.

In his large and extremely careful follow-up investigation of 330 patients treated on these principles during the years 1913-1932 at the orthopedic clinic in Stockholm, Severin (1941) found an anatomically normal joint in only 4.2%. In no less than 73.7%, some degree of subluxation or dislocation was found.

About 1937, Waldenström introduced in Stockholm the method of commencing treatment as soon as the diagnosis was made, preferably before the age of one year. This consisted of plaster fixation of the hip joint alone (not, as previously, including the knee and foot joints), on both sides, since it was found that the tendency to dislocation was often bilateral. This improved the results considerably, and anatomic healing was found in 30% of the cases after an observation period of at least 5 years.

Early Diagnosis and Treatment

Even if, as previously mentioned, Lorenz's principle of postponing reduction until the second or third year of life was generally accepted, there were those who during the first decades of the 20th century spoke in favour of early treatment.

As early as before 1910, Froelich (1932) of Nancy observed that the tendency to dislocation could be diagnosed during the first week of life, and that it was then possible, if a dislocation were found, to reduce the femoral head by abducting the legs in the deflected hip joints. He considered that the earlier the commencement of treatment, the better the results, and that before the age of one year good results were always obtained. These observations were reported by Froelich to the French surgical congress in 1911, and were also published by his pupils Hoffman (1911) and Vuillaume (1910) (cit. Froelich 1932). Early treatment of infants was not accepted, however, according to Froelich because of opposition from leading orthopedists.

Joachimsthal (1908) and Peltsohn (1920) treated six infants in 1909, and the latter, in a publication in 1920, opposed the general view that reduction should be postponed until the second or third year. He considered that the most favourable time was past even when the child had begun to walk, and he sought an improved diagnosis and suggested that the doctor attending a delivery should examine the hip joints of all newborn children.

Many others have described individual cases of early reduction, and have urged early diagnosis and treatment. (Loeffler, Frauenthal, Engelmann (cit. Hilgenreiner 1925), Hohmann 1935).

Hilgenreiner (1925) of Prague reported a case of bilateral dislocation in a 12 day old girl, who later died of pneumonia at the age of 4 weeks, where the autopsy revealed only extremely flat acetabula. He considered the cause of dislocation to be a congenital "Hemmungsbildung",

which includes the whole joint and its surrounding tissues, and that all stages may be found, from the normal to complete dislocation. He suggested the name "dysplasia" with or without dislocation. Hilgenreiner used an aluminium abduction splint for early treatment. In 1935 he presented 157 cases treated under the age of one year, including two in their second month. He described here the reduction sound and that of the relaxation, which is particularly easily heard in infants of 3-6 months. He considered that the treatment should preferably be commenced at the age of 4-6 months, with an abduction splint.

In Italy attention was directed to dislocation of the hip at an early date because of the high frequency of this disease in certain provinces, and early treatment was introduced there by Putti of Bologna, who from 1921 onwards continually strove for treatment before the age of one year. At an orthopedic congress in London in 1929 he presented his first 24 cases (Putti 1929), all treated with good results with a simple abduction position by means of a pillow placed between the legs. In 1933 he reported the further experiences from 119 early treated cases (Putti 1933). He introduced the concept of "predislocation" for those cases where the roentgen picture showed an increased acetabular roof angle, but where subluxation had not yet occurred. The youngest case treated in this material had such a predislocation and was 34 days old, and the oldest was 16 months old. The result was stated as being a "complete cure" in 113 of the 119 cases. Putti considered that treatment should begin the very moment the deformity is observed, even if that be on the

day of birth. To achieve this aim he suggested that roentgen pictures should be taken of the hip joints of all newborn children as a routine practice.

Ortolani of Ferrara maintained in 1935 that the reduction sound which had long been observed by orthopedic surgeons could also be obtained in infants who had only a subluxation, that is, where the femoral head had not gone over the acetabular edge. He stated that this "click" was the deciding factor for the diagnosis in infants, X-ray examination was uncertain before the epiphyseal nucleus could be observed in the femoral head, and that all with this symptom should be treated with the abduction position by means of a pillow placed between the legs. Ortolani has in many publications, including a monograph in 1948 (Ortolani 1948), urged early diagnosis and treatment as soon as the diagnosis is made. He has organized a "diagnostic and prophylactic centre for dislocation of the hip" in Ferrara. Since in Italy about 75% of child deliveries take place in the home, Ortolani has trained nurses to examine the children during their home visits as early as possible with respect to "the click". Between 1935 and 1951 Ortolani treated over 2000 cases (Ortolani 1951), and since 1951 has also treated about 200 new cases annually. Unfortunately his earlier publications of 1930-1940 did not, as they deserved, attract the attention of the pediatricians and orthopedic surgeons, and his principles of early diagnosis and treatment spread only very slowly in the rest of Europe.

Frejka (1941) of Brno adopted the treatment with an abduction pillow between the legs, and suggested such treat-

ment for all newborn children (a) with dislocation in the family, (b) which were delivered in the breech position, and (c) with limited abduction. This abduction pillow, which has also been used previously, among others by Ortolani, has come into use under Frejka's name in different countries, including Sweden.

In the U.S.A. Chapple (1935) stated that he had treated three infants in their first three months with a "splint", with good results. He pointed out that congenital dislocation of the hip was an important pediatric problem which had been previously neglected because it was not realized that as a rule there is no dislocation but only the absence of an ossified acetabulum.

During the 1940's Hart of Minnesota advocated early treatment, and presented his views in a monograph in 1948 (published posthumously, Hart 1952). There he describes dysplasia as a stage of preluxation in the newborn, and gives an account of Ortolani's method of examination and early treatment with the Frejka pillow. No report is made, however, of any examined or treated cases.

Even if, as is evident from the above, it was realized by many before the 1950's that diagnosis of "dysplasia" of the hip joint was possible even in the newborn, not until that period was this method of examination of the hip joints adopted in the routine examination of all newborn in the obstetric clinics.

In the autumn of 1950 I began the investigation, the results of which are presented here, and I made a preliminary report in 1953 (Palmén 1953).

Attention has been paid to my reports of 1953 and 1957 in the other Scandinavian

countries, and routine examination of all newborn children has been reported from different places.

In Bergen in Norway all the newborn were examined from 1953 onwards (Walther and Moe 1954), at the Universitets-Frauenklinik in Würzburg from August 1952 (Burger 1953, Penners 1955, Bayer 1958)

and at the Universitets-Frauenklinik in Zürich from 1959 (Geschwend 1959).

In the U.S.A. these examinations have taken place, for example, in Salt Lake City from 1956 onwards (Coleman 1956) and at the Mayo Clinic in New York from 1960 (Harris *et al.* 1960).

INTRODUCTION

In August 1950 I noticed an article on "congenital dislocation of the hip in the newborn" by Hart (1950), in which he describes Ortolani's examination method and treatment with an abduction pillow. I then introduced this hip joint examination into the routine examination of all the newborn at the obstetric department of the Central Hospital in Falköping, where I am the pediatric consultant. This hospital is a central hospital for approximately 125,000 inhabitants as regards obstetrics and pediatrics, and has about 1200-1300 deliveries per year.

I found the first case with an Ortolani click in December 1950, and a further 4 cases during 1951-1952. As a result a circular letter was sent in December 1952 to all consultant pediatricians at the obstetric clinics in Sweden, suggesting that from January 1st, 1953, they should include Ortolani's examination method in their routine examination of all the newborn. This examination had already been introduced in a few places, and all consultants written to were interested, and have since willingly given me access to their material.

During the first years of the investigation, between 1950-1952, I examined in Falköping 2231 newborn children. In the whole country hip joint examinations

were made on 33,681 in 1953, corresponding to 31 % of all children born in Sweden during that year. During the following years some further hospitals were added, so that during 1960, 68,000 newborn children were examined, corresponding to 67.4 % of all children born in that year in Sweden. Also, during the last few years a further large percentage of those children born in other smaller hospitals and cottage hospitals have also been examined, but no record of these cases has been made.

In order to spread information concerning the examination of the newborn, I published articles in the Swedish Medical Journal (*Svenska Läkartidningen*) in 1953 and 1957 (Palmén 1953, 1957), in the Journal for Swedish Nurses (*Tidskrift för Sveriges Sjuksköterskor*) in 1957 and in a journal for midwives (*Jordemodern*) in 1957.

In 1957 a circular was sent out by the National Board of Health, at my suggestion, to all physicians at the obstetric departments and other maternity institutions in the country with a recommendation to introduce hip joint examination of all newborn children. This memorandum was accompanied by reprints of the above-mentioned article in the Swedish Medical Journal of 1957, where the method of examination was described in detail.

The Aim of the Investigation

The aim of the present investigation is as follows.

I. To attempt to elucidate the possibilities of diagnosing congenital hip preluxation in the newborn, to define this disease condition in the newborn, and to ascertain its relation to dislocation of the hip joint.

II. To study whether most cases which left untreated might be expected to give rise to dislocation during childhood may be effectively discovered by diagnosis in the newborn.

Since in Sweden 98.9 % (1958) of all births take place in obstetric clinics, and probably practically all cases of luxation are treated in orthopedic clinics, there should be good prospects in Sweden of elucidating this

problem by recording over a series of years those cases of hip joint preluxation diagnosed at the obstetric institutions, and also all cases of dislocation which are treated at the orthopedic clinics. It should also be possible, for the latter cases, to record the obstetric clinic at which the child was born. By comparing these groups a good idea should be obtained of the extent to which cases of preluxation can be discovered as early as in the newborn, and how great a percentage pass the examination at the obstetric clinic as healthy, to be diagnosed later as dislocation. It should also be possible by this investigation to show how the diagnosis and treatment of newborn children influence the frequency of dislocation of the hip during childhood in this country.



PART I

Diagnosis and Treatment of Preluxation in the Newborn

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I. MATERIAL

From the 1st September 1950 to the 31st December 1960, the routine examination of all newborn children at the Obstetric Clinic of the Central Hospital of Falköping included an examination of the hip joints. This examination was made by the author in about 11,000 cases, and by carefully instructed deputies in the rest, i.e. about 1400 cases. The newborn children were examined in the following way.

I. By the abduction manoeuvre described by Ortolani. In 1956 this manoeuvre was complemented with a subluxation provocation.

II. By roentgen photography of the hip joints of the cases found to be positive on these examinations.

Number of newborn examined: 12,394 (see Table 1 for distribution into years). Of these, 520 premature children who were born at the obstetric department and immediately transferred to the pediatric clinic were examined there. In most cases the children were examined only on one occasion between the 1st and 4th day of

life. Uncertain cases were examined more than once, at intervals of a few days.

TABLE 1. *No. of cases of preluxation of the hip joint diagnosed at the Obstetric Clinic of the Central Hospital in Falköping during the years 1950-1960.*

A, no. of newborn children examined.

B, no. of cases who exhibited subluxation by Ortolani's click sign.

C, no. of cases who showed signs of preluxation only on subluxation provocation.

D, total no. of cases.

Of the 46 cases in group B, 36 were girls and 10 boys; of the 24 cases in group C, 21 were girls and 3 boys; of the total 70 cases, 57 were girls and 13 boys, i.e. 4.4:1.

Year	A	B	C	D
1950	320	1		1
1951	906	3		3
1952	1005	1		1
1953	1185	2		2
1954	1170	2		2
1955	1227	5		5
1956	1249	6	2	8
1957	1285	10	7	17
1958	1368	6	5	11
1959	1357	8	6	14
1960	1322	2	4	6
Total	12,394	46	24	70

II. CLINICAL EXAMINATION

The Examination Technique

The abduction manoeuvre described by Ortolani, which is based on the fact that by means of the laxity of the hip joint it is possible to reduce an existing subluxation with ease.

The child lies on its back on an examination table. The examiner stands at the foot.

Stage I. The legs are first extended straight and adducted close to one another, and one leg is then taken in each hand with the thumb against the inside of the distal part of the thigh and the other fingers on the outer side so that the first and middle fingers press against the trochanteric region. The hip and knee joints are deflected to 90° , with the legs still adducted (Fig. 1a).

Stage II. The knees are bent down towards the examination table (=abduction of the hip joints), and at the same time *slight* pressure is exerted both in the direction of the femurs in towards the hip joints and also forwards and upwards with the fingers placed against the trochanteric region. In a normal hip joint it is easily possible to abduct 90° , if the child is almost relaxed. If a subluxation or luxation is present, slight resistance is felt when 45° – 60° is reached during the abduction movement (Fig. 1b), and when this resistance is easily overcome, a dis-

tinct click in the hip joint is perceived—in most cases one can both feel, hear and see the femoral head slipping into the acetabulum forwards and upwards. It is then easily possible, without resistance, to continue the abduction to 90° (Fig. 1c).

Stage III. If from this position adduction is performed by *slight* backward pressure (dorsally) on the proximal part of the femur, the same phenomenon is again obtained, when the femoral head once more "reluxates".

In 1956 I made the observation (Palmén 1957) that in a number of cases, where with Ortolani's abduction manoeuvre no click is produced, it is nevertheless possible to displace the femoral head backwards (dorsally), i.e. a *subluxation may be provoked*. This method of examination is also used by Coleman (1956). For reasons which will be given later, I have concluded that in such cases there is a preluxation of the hip joint of the same type. The examination was thus complemented with Stage IV.

Stage IV. From a basic position of 90° flexion and slight abduction (about 45°), the legs are held as in stage I, but with the thumbs further up against the upper femoral ends, and moderate backward pressure is exerted (dorsally), at the same time as slow adduction and slight inward rotation are carried out, as if the femoral head were to be luxated (Fig. 2). In cases

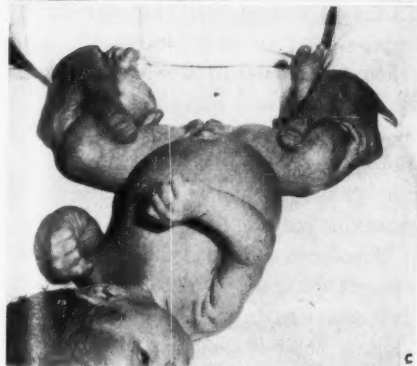
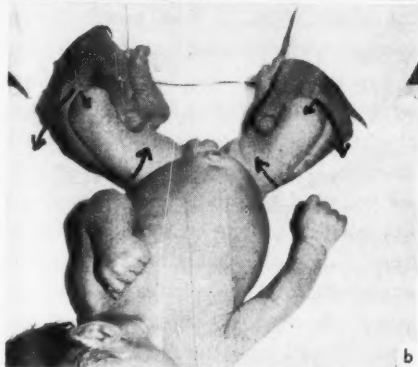


Fig. 1. The abduction manoeuvre. (a) stage I, (b) stage II, (c) stage III.

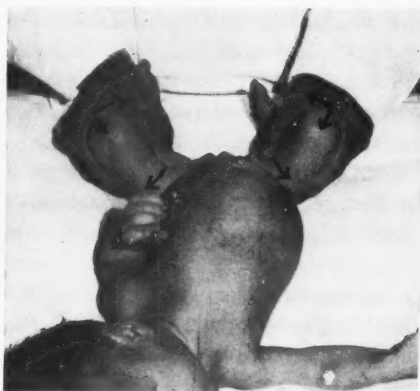


Fig. 2. The subluxation provocation.

of prelaxation a distinct displacement of the femoral head outwards on to the posterior acetabular edge may then be felt. If pressure is then exerted by the fingers placed against the trochanteric region, the femoral head may again be replaced, with a more or less distinct click, into its reduced position. This stage is best carried out on one leg at a time. The other hand has the same hold, but supports instead the pelvis.

Discussion on the Examination Technique

During the first week of life the muscles of a child are as a rule rather relaxed, and it is therefore easiest to perform the hip joint examination during this period. After one to three weeks, many children physiologically have an increased tone in the adductor muscles, and it is then no longer as easy to carry out the examination. It is probably then even more difficult to establish mild cases of prelaxation according to stage IV. It is important

that the child is calm and relaxed during the examination. If it cries or is apprehensive, the adductor muscles become taut and abduction should not then be forced against resistance. It is usually easy to calm the child by giving it a bottle or pacifier, or otherwise the examination should be postponed until a later occasion, e.g. after a meal.

In these cases there is often an abnormal flaccidity or hypotonia in the joint. Preluxation may be suspected simply by the resting position of the child, with one or both legs lying relaxed in 90° flexion and 90° abduction. This was so in two of my cases. This abnormal laxity in the hip joint is also felt as soon as the leg is held. In these cases it is especially important in the abduction manoeuvre to press the femoral head slightly against the acetabulum in order to perceive the click more easily.

In many cases of subluxation, when the abduction manoeuvre is performed for the first time the click may be less evident, and there may be slight resistance. If, however, the examination is repeated a few times it becomes easier, and the click is so distinct that it is both "seen" and heard even by people standing nearby. This perhaps depends on the fact that the negative pressure holding the femoral head fast in the acetabulum is overcome. The abduction manoeuvre should subsequently be repeated immediately a few times.

It is no doubt advisable, however, not to repeat the examination unnecessarily, after a click is once established, since the tissues of the hip joint, especially the cartilage and ligaments, may become damaged.

I believe that it is important in the ex-

amination to start from the basic position with extended, adducted legs, as mentioned in stage I. If the child lies in the "physiological resting position" with the legs deflected 90°-110° and abducted 80°-90°, a possible subluxation can be reduced, and if from this position the legs are carefully adducted—still with retained flexion—and then abducted again, it is possible that no click will be perceived. The femoral head would rotate upon adduction-abduction in its reduced position. It is important, then, in these cases, that the subluxation is first manifest in a position with extended and adducted legs.

In some cases with strongly pronounced hypotonia in the hip joints, I have made the following observations which seem of interest. If, with the child lying with the leg deflected and abducted 90°, the leg is extended by pulling on the foot, with the knee sliding the whole time against the examination table, a click can be distinctly perceived when a position of about 45° abduction of the extended leg is reached. In the starting position the subluxation is reduced, and the click which is felt occurs when the femoral head relaxates because of adduction and some inward rotation. With extended adducted legs the subluxation is then manifest, and it is retained if the abduction manoeuvre is commenced from this position (stage I).

The above is a good illustration of the observation made by Ortolani and others, that luxation is more common in those regions where it is customary for mothers to have their infants lying with the legs straight and bound together. It is also a possibility, that the modern use of disposable diapers with plastic knickers may constitute some degree of prophylaxis

against dislocation in mild cases of preluxation, as this means a position of abduction.

Results of the Clinical Examination of the Hip Joints of all Newborn at the Obstetric Clinic of the Central Hospital in Falköping

During the years from September 1950–December 1960 in which the investigation was carried out, out of 12,394 newborn children examined, 70 cases of preluxation were diagnosed (one case of a complete luxation is included), distributed according to Table 1. Forty-six cases (10 boys, 36 girls) showed a positive Ortolani sign, indicating subluxation. Also, from 1956, 24 cases (3 boys, 21 girls) showed positive symptoms only on subluxation provocation (stage IV in the manoeuvre).

Out of the 55 cases where both the abduction manoeuvre and subluxation provocation were performed, 26 (47.3%) had positive signs on both sides and 29 had unilateral subluxation or signs of preluxation on subluxation provocation on only one side:

Cases with positive signs on both sides

Subluxation	9	} Total 26
Positive subluxation provocation	7	
Sublux. sin. + provocation dx.	6	
Sublux. dx. + provocation sin.	4	

Cases with unilateral subluxation or signs of preluxation on subluxation provocation

Subluxation sin.	11	} left side 27	} Total 29	
Provocation sin.	16			
Subluxation dx.	1	} right side 2		
Provocation dx.	1			

This material is of course much too small for calculating any statistically significant frequency figures. On the whole

material, however, i.e. 12,394 newborn examined, the frequency of preluxation with or without subluxation was 5.7%. The frequency of cases which by the abduction manoeuvre described by Ortolani showed signs of subluxation, was 3.8%. The frequency of further cases of preluxation, diagnosed by means of subluxation provocation, was 4.2%.

In an investigation of the number of children who during the years 1936–1945 were admitted to orthopedic clinics in Sweden before the age of 5 years, Severin (1956) found a frequency of 0.9%. The frequency of preluxation found in the present investigation is considerably greater than the frequency of dislocation found by Severin. The presumed reasons for this discrepancy will be discussed later.

Other Clinical Symptoms in the Newborn

It has long been the practice in examining the newborn to look also for those symptoms which are important in the diagnosis of luxation in older children: limited degree of abduction, leg shortening and different signs of asymmetry, especially of the medial thigh folds. Since these symptoms are expressions of an already existing luxation, or at least a high degree of subluxation, it cannot be expected that they will be found other than in those rare cases, where such a condition is already present at birth.

If there is complete luxation, the child usually lies with the luxated leg adducted and more or less deflected, and exhibits markedly less active movement in the hip joint. In unilateral cases there is usually obvious leg shortening. Often in these cases

no distinct click is perceived during the abduction manoeuvre, due either to the fact that because there is already an adduction contracture the luxation cannot be reduced, or that the femoral head rotates completely outside the acetabulum during abduction. These cases, which are generally considered to constitute about 2% of a luxation material, as a rule have a malformed acetabulum, which is small and flat, and a rather small, deformed femoral head, and are therapeutically unfavourable. These conditions are usually combined with other malformations, such as pes equinovarus, luxation of the knee joint, spina bifida and arthrogryphosis multiplex.

The only symptom of those mentioned above, to which importance need be attached when examining the newborn, is *limited abduction*. As mentioned previously in the description of the examination technique, increased laxity in the joint is often found in cases of preluxation, but in a number of cases some resistance may be felt during the abduction manoeuvre, an obstruction to the abduction, at 45°–60°, which can easily be overcome, however. More marked limitation of abduction is unusual in preluxation in the newborn, but should arouse suspicion of luxation if observed in a child who is otherwise relaxed. Oldfelt and Magnusson (1952) diagnosed luxation in 3 newborn children, this being verified by roentgen examination after abduction limitation had aroused suspicion.

Attempt has been made to classify abduction limitation and determine the normal boundary values. Harris *et al.* (1960) from the Mayo Clinic, for example, found normal abduction to be 80°–90° in the newborn, and 60°–70° at the age of 1–9

months. They considered that an abduction of only 50°–60° should arouse suspicion of luxation, and should be further investigated by roentgen examination of the hip joints.

As mentioned previously, there is a physiological increase in the adductor muscle tone as early as at the age of a few weeks, manifested by a more or less limited degree of abduction, especially when the child is alert and makes avoiding movements during the examination. It may be difficult, therefore, to assess this abduction resistance, but since it is one of the most important signs of luxation later during the infant year, I have chosen to mention it here. If, on repeated examinations, there is constant resistance to abduction before about 60°, when the child is relaxed, luxation should be suspected.

Much has been published previously concerning *asymmetry of the skin folds*, especially that on the medial side of the thigh; the majority now agree that this is an uncertain sign in the newborn, but it is still mentioned as one of the early signs.

In order to study the degree of abduction possible and the medial thigh folds in the newborn, I examined 500 newborn children, all being children born alive during a consecutive period of 5 months. This investigation revealed that, of the newborn, 27.6% had no medial thigh folds at all, 39.6% had symmetrical folds, and 32.8% had asymmetrical folds. 44.7% of those with a birth weight of under 3400 g had no folds. 70% had an abduction of 90°–100°, 28% had a maximal abduction of 80°, and 2% had a maximal abduction of 70°. None of the 500 children examined had an abduction of less than 70°. Among these, 4 were found to have preluxation:

none of these 4 had less abduction than 90° , two had symmetrical folds, and of the other two, the medial thigh fold of one was 3 mm higher on the subluxated side, while that of the other was 3 mm lower.

Since, as is evident from this investigation, the normal variations are so great, the examination of the medial thigh folds in the newborn is of no value in making the diagnosis of preluxation.

III. ROENTGEN EXAMINATION

General Aspects

Roentgen examination of the hip joints in newborn and infant children during the first months of life is subject to special difficulties and sources of error.

During these months the epiphyseal nucleus in the femoral head consists only of cartilage, and is therefore not visible in the roentgen picture. The acetabulum also consists mainly of cartilage, the ossified part of the acetabulum on the ilium is still poorly developed, and often shows a somewhat diffuse boundary line on the roentgen picture.

The capital nucleus is normally ossified at about 4 months, but sometimes not until some months later, and, as has long been known, in cases of luxation often considerably later. When the nucleus of the femoral head is ossified, it is easier to see a possible subluxation or luxation on the roentgen picture.

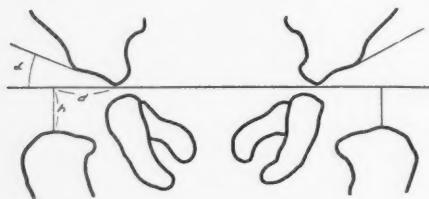


Fig. 3. Hilgenreiner's measurements. h = distance between the Y line and the highest diaphysis point. d = distance from the highest diaphysis point, measured on the Y line, and the point where the Y line and acetabular line cut one another. α = angle of the acetabular roof.

Another important problem which renders the assessment of the roentgen picture more difficult, is that of obtaining symmetrical alignment of the femora and pelvis during the exposure.

The method which has long been in general use in roentgen examination of the hip joints in infants, is that described by Hilgenreiner (1925), using an anterior-posterior picture with extended adducted legs. Hilgenreiner constructed some auxiliary lines on the roentgen picture (see Fig. 3), and with their guidance assessed any possible deviation of the cranial femoral end, cranially and laterally, and also the acetabular index, i.e. the angle formed by the Y-line and a line drawn through the visible osseous part of the acetabulum. In unilateral subluxation or luxation, the h -distance is smaller and the d -distance greater on the affected side, compared with the other side, and in bilateral cases these values deviate considerably from certain normal values. In cases of dislocation the acetabular index is greater than the normal value, and a greater angle alone has been considered to indicate "dysplasia", or "presubluxation" (Putti 1933). By examining a large number of newborn children, attempt has been made to obtain the normal values with the measurements mentioned (Hilgenreiner, Faber 1938, *inter alia*), but the values given show great variations, and the measurements were made directly on

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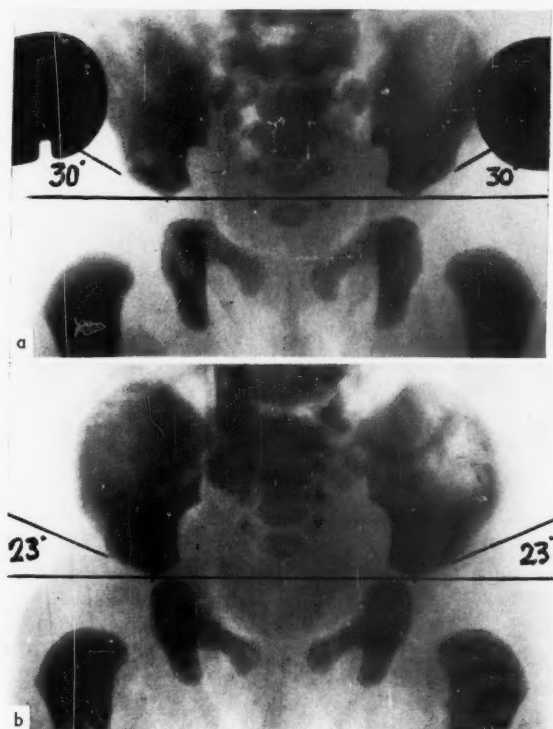


Fig. 4. The effect on the acetabular angle of pelvic rotation. (a) the pelvis in only slight lordosis; the angle is 30°. (b) the pelvis in increased lordosis; the index has become smaller (23°).

the roentgen pictures, but no information was given concerning the enlargement. Neither were the children divided into different groups according to size (birth weight and length), and, most important of all, nothing was mentioned regarding the symmetrical positioning of the pelvis.

Perhaps the greatest source of error when making these measurements is the difficulty mentioned above of keeping the child in an exactly symmetrical position. A pelvic rotation affects the acetabular angles; if the child lies with increased lordosis in the lumbar spine the angle be-

comes smaller, and a rotation of the pelvis from one side to the other also affects the angle. The effect of different pelvic positions on the acetabular angle may be seen in the roentgen pictures in Figs. 4 and 5.

The assessment is also more difficult if the position of the legs is asymmetrical. In many cases the acetabular borderline is so diffuse that the drawing of this angle line becomes rather pointless.

In cases of luxation or marked subluxation, such an obvious difference in Hilgenreiner's *h*- and *d*-distance can be obtained that there need be no doubt about the

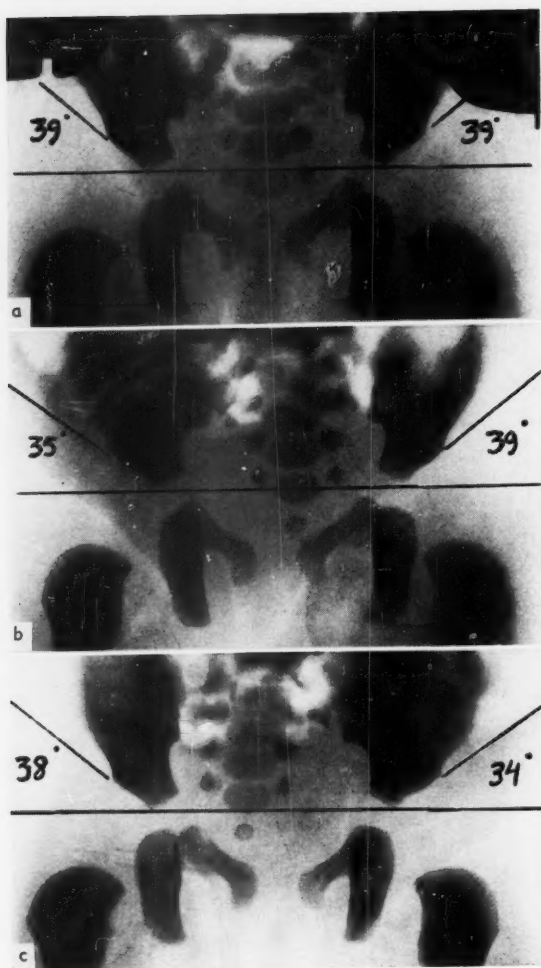


Fig. 5. The effect on the acetabular angle of pelvic rotation. (a) the pelvis in symmetrical position. The right and left angles are the same (39°). (b) the pelvis rotated towards the right: the right angle is smaller (35°). (c) the pelvis rotated towards the left: the left angle is smaller (34°).

diagnosis—if the position is at all symmetrical. In the small subluxations which are often found in the newborn (a few mm only), no definite diagnosis can be made by a roentgen picture taken as described above—especially in cases of bilateral small

subluxations or if the roentgen picture is taken somewhat asymmetrically.

To attempt to avoid sources of error caused by an asymmetrical position and different degrees of lordosis, I constructed a small table (Fig. 6), to which the new-

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Fig. 6. The table used for the roentgen examination of the newborns in symmetrical position.

born child could be strapped with its legs adducted, and with the hip joints flexed at 30° (to counterbalance the lumbar lordosis). The pelvis could be fixed by means of a support placed against the region of the iliac crest, and which could be screwed in symmetrically from the sides and from top to bottom. A further advantage of this arrangement was that the assistants did not need to hold the child, and were therefore not exposed to roentgen radiation.

In order to obtain an idea of the adequacy of this method, I made roentgen examinations of 80 newborn children, 40 boys and 40 girls, with birth weights varying between 2650 g and 4400 g, and on these pictures I measured the d - and h -distances and the acetabular angle. The roentgen tube was centred against the symphysis pubis, and the distance from the focus to the roentgen cassette was 90 cm.

It was found that in those cases where the position was exactly symmetrical, the h -distance did not vary more than 0.5

mm compared with the other side, and the d -distance 1 mm. It is more difficult to measure the d -distance on the roentgen picture, since the lateral placing of the h -line is sometimes rather uncertain—it should be drawn from the highest point on the femoral end.

In about 50% the positions were not exactly symmetrical, and in these the variations were somewhat greater, being up to 1.5–2 mm.

The d - and h -distances vary to some extent depending on the size of the child, the differences between the smallest and the largest children being about 2 mm.

As previously known (Hilgenreiner, Faber, *inter alia*), the acetabular angle is greater in girls than in boys. The variations were rather great, i.e. 28° – 40° (mean value 36°) in the girls and 25° – 38° (mean value 31°) in the boys with the above-mentioned fixation in 30° flexion. The variations seem to depend mainly on the differences in pelvic slope due to different degrees of lordosis, while the size of the child hardly seems to affect the angle.

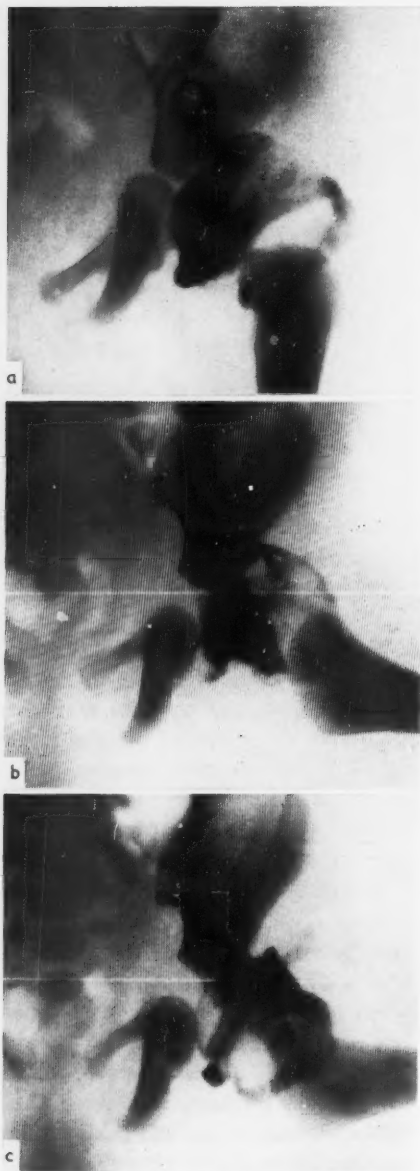


Fig. 7. Arthrography in a newborn child with subluxation. (a) subluxation in a position with the leg extended and adducted. (b) subluxation just before the click. (c) completely reduced position after the click. Note the difference in the distance from the femoral end to the ischial bone: in (b) 13 mm, in (c) 10 mm.

The material is, of course, too small to allow a careful statistical analysis and the establishment of normal values for different size groups of newborn children. For reasons which will be given later, I have not, however, extended this material for such purposes. I have nevertheless chosen to use this investigation in order to throw some light on this method of roentgen examination, and above all its sources of error.

The fixation arrangement described has been used since May 1957 for the roentgen examination of the 39 cases diagnosed after this date. It has been found to serve its purpose well, and is a definite improvement on the times when the assistants had to hold the children, as in the first 31 cases.

Roentgen Examination of the Clinically Diagnosed Cases

All 70 cases were examined roentgenologically, an anterior-posterior picture being taken with extended, adducted legs, with the roentgen tube centred against the symphysis pubis and with a distance of 90 cm from the focus of the tube to the cassette. In 36 cases further special pictures were taken, and the material can therefore be classified into three groups.

Group I: 34 cases with only the above-mentioned anterior-posterior picture, and also, in a number of cases, a picture with the legs in 90° flexion and 90° abduction.

Group II: 18 cases (during the years 1953-1957). The above-mentioned anterior-posterior picture and also two further pictures, one with the legs in 90° flexion



Fig. 8. A case of total luxation (case no. 16) with marked cranial displacement of the femoral ends.

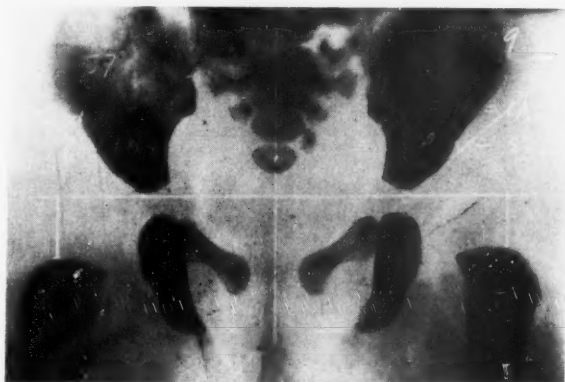


Fig. 9. A case of left-sided subluxation. Symmetrical position. Hilgenreiner's measurements: on the right side, $d = 15$ mm, $h = 10.5$ mm, angle = 37° ; on the left side, $d = 17.5$ mm, $h = 8.5$ mm, angle = 39° .

and 45° - 60° abduction—just before, and the other in the same position just after the click. The distance from the femoral end to the ischial bone was measured on these pictures.

Group III: In 18 cases (during the years 1958-1960), apart from the first-mentioned anterior-posterior picture, a further picture was taken with the legs extended, 45° abducted and inwardly rotated. This position was described in 1958 by Andrén and von Rosen (1958), who considered

that luxation could best be diagnosed by this means. If a line is drawn on this picture through the longitudinal axis of the femoral shaft, its extension meets the region of the anterior-superior iliac spine in cases of dislocation, while in a normal joint it points towards the acetabulum.

Most cases were examined roentgenologically by the author personally, these including all the cases in the last two groups.

In one case an *arthrography* was also

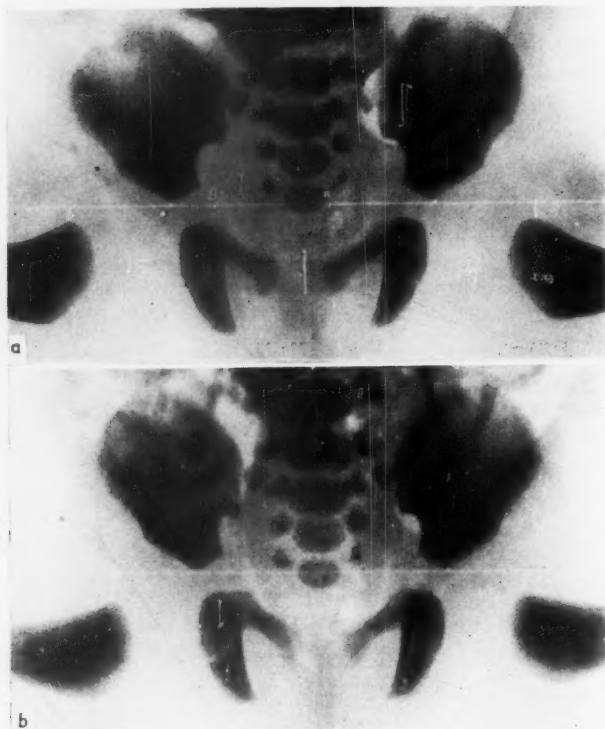


Fig. 10. A case of bilateral subluxation immediately before (a) and after (b) the click during the abduction manoeuvre. The distance from the femoral end to the ischial bone has decreased from 15 and 14 mm respectively to 11 mm.

performed, where the clinically diagnosed subluxation and the normal, reduced position after the click could be observed clearly (Fig. 7). Since in the newborn, arthrography requires anesthesia and means a certain degree of risk for the child, I did not use this method further. I also attempted to limit other roentgen examinations as much as possible, so that the newborn children were not subjected to excessive roentgen radiation.

Results of the Roentgen Examination

The criteria for positive roentgen findings—with exactly symmetrical positioning of the pelvis on the film—were as follows.

Group I: A difference in *h*- and *d*-distance of at least $1\frac{1}{2}$ mm compared with the other side in unilateral cases. In bilateral cases a distinct cranio-lateral deviation of the femoral ends—the *h*- and *d*-distance—more than 2 mm smaller or greater, re-

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Fig. 11. A case of left-sided subluxation. The legs are abducted and inwardly rotated, and it has been felt clinically in this position that the left femoral head has just subluxated.

spectively, than the boundary values in the normal material.

Group II: A difference of at least $1\frac{1}{2}$ mm in the distance from the femoral end to the ischial bone before and after the click.

Group III: The extension line through the femur should meet the ilium outside the acetabulum.

Group I: Of the 34 cases 1 showed a total luxation (Fig. 8); this was combined with bilateral pes. equino-varus, and hydrocephalus also developed later. Nine cases had subluxations (example in Fig. 9). Twelve were assessed as uncertain, when the difference in the *h*- or *d*-distance was not more than 1 mm, or when the *h*-distance in bilateral cases was not definitely decreased. In 12 cases the position was asymmetrical (the pelvis somewhat rotated). Two of these cases, however, had definite subluxations shown by a decreased *h*-distance.

Group II: Of the 18 cases, 13 exhibited

distinct subluxation before the click, and this was afterwards reduced. Of these, 3 were bilateral cases, which showed a difference of 3-4 mm before and after the click (Fig. 10).

Of the remaining 5, 2 were markedly asymmetrical. In 1 case the difference was only 1 mm, and in 1 case the pictures were lost. In only 1 case was there any difference before and after the click. This was clinically a left-sided prelaxation at the subluxation provocation.

Group III: Of the 18 cases examined, 17 displayed signs of subluxation (example in Fig. 11). Only in 1 case was the roentgen picture normal in this position—this was clinically a case of left-sided prelaxation at the subluxation provocation.

The roentgen examination in the 55 cases where the positioning on the film was symmetrical thus revealed 39 subluxations and 1 total luxation, 13 uncertain cases and 2 negative cases.

IV. COMPARISON BETWEEN THE CLINICAL AND THE ROENTGEN EXAMINATIONS

It is of great interest to observe whether the roentgen examination, performed in the different ways mentioned above, agrees with the clinical examination, not least in those cases where the latter revealed signs

TABLE 2. *Comparison between the clinical and the roentgen examination in the 55 cases where the positioning of the pelvis on the film was symmetrical.*

- A, bilateral subluxation by the abduction manoeuvre.
B, unilateral subluxation by the abduction manoeuvre.
C, bilateral preluxation by the subluxation provocation.
D, unilateral preluxation by the subluxation provocation.
E, unilateral subluxation + preluxation on the other side by the subluxation provocation.
F, total no. of cases.

	A	B	C	D	E	F
<i>Group I</i>						
No. of cases	6	5	3	7	1	22
Roentgen "pos." bilat.	3					10
Roentgen "pos." unilat.		2	1	4		
Roentgen uncertain	3	3	2	3	1	12
Roentgen negative						0
<i>Group II</i>						
No. of cases	2	8	1	1	3	15
Roentgen "pos." bilat.	2		1		1	13
Roentgen "pos." unilat.		7			2	
Roentgen uncertain		1				1
Roentgen negative				1		1
<i>Group III</i>						
No. of cases	3	1	1	6	7	18
Roentgen "pos." bilat.	2		1		3	17
Roentgen "pos." unilat.	1	1		5	4	
Roentgen uncertain						0
Roentgen negative				1		1

of preluxation only by means of subluxation provocation.

This comparison is shown in Table 2 where the 55 cases on whom the position was symmetrical, so that a definite assessment was possible, are included.

As may be seen in the table, in Group I where the legs were extended and adducted, only in about half of the cases were the roentgen findings definitely positive.

In the other two groups, where a roentgen picture was taken in a position in which subluxation of the femoral head could be clinically felt, the roentgen examination showed very good agreement with the clinical examination. This, of course, is only what could be expected.

It was of especial interest that in the 19 cases, where preluxation was only diagnosed clinically by means of subluxation provocation, the roentgen finding was positive in 12 cases. In the 9 cases examined in Groups II and III, the roentgen finding was positive in 7 cases.

In 11 cases with clinical subluxation of the one side and only provocation subluxation on the other, the roentgen finding was also positive for the latter side in 4 cases, and probable in a further 3 cases.

Finally, a few words may be mentioned here concerning the measurement of the acetabular angle according to Hilgenreiner. As mentioned previously, the examination of the normal material revealed great

variations, the angle varying between 25° and 40° , depending mainly on varying pelvic positions, but also depending on the difficulty in drawing the angle line from the Y-line through the osseous part of the acetabulum visible on the roentgen picture.

The acetabular angle was measured in all 70 cases. In only 9 cases was it greater than 40° (the greatest value in the normal material), and no definite relationship between this angle and the other roentgen findings, or the clinical examination, could be established.

V. THE TREATMENT OF PRELUXATION IN THE NEWBORN

As soon as the diagnosis was made at the clinical examination in the obstetric department between the 2nd and 4th day of life, the children were transferred for treatment to the infant department of the pediatric clinic, which is situated in the same building, so that it was possible for them to be breast-fed as usual.

In 3 of the first 5 cases diagnosed during the years 1950-1952 no treatment was given from the beginning, the roentgen examination revealing no definite dislocation, as far as could then be judged.

Of the remaining 67 cases all, with the exception of 2 "slight" cases, were treated by means of fixation on a wooden board with the legs in a position of 90° - 110° flexion, and with 80° - 90° abduction in the

hip joints. Various types of wooden boards were tested, and that shown in Fig. 12 was found to be the most suitable. This was used in the last 30 cases.

The child lay on a piece of foam rubber on the wooden board, wearing an ordinary disposable diaper. Usually another piece of foam rubber was placed under the knees, to avoid too great a degree of abduction. The child was secured by means of webbing straps.

An aluminium abduction splint was also constructed (Fig. 13); this was tested in two later cases and found to be satisfactory. This splint is easy to apply, gives good fixation of the legs, and also it is possible to change the child's diaper without having to remove the splint. The degree of abduction can be varied by bending the

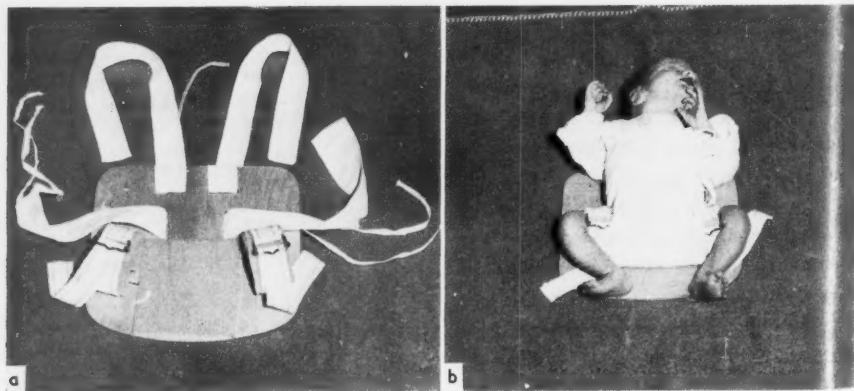


Fig. 12a and b. The wooden board used for the fixation treatment.

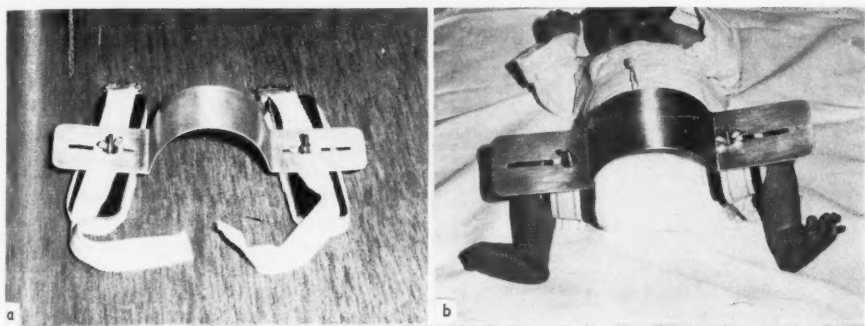


Fig. 13a and b. The aluminium abduction splint.

splint, and the fixation device can be adjusted to fit children of different sizes. Further experience will possibly show that this splint is to be preferred to the wooden board.

In many cases, as mentioned previously, there is increased flaccidity in the joints, and it is then possible to abduct the legs to 90° without the slightest resistance. In a few cases some resistance to abduction was encountered from the beginning. In those cases the child was placed in a position of slight abduction for the first 24 hours, and this was then increased as the muscular tension became more relaxed. After about two days, abduction to 90° was always easily possible.

The child remained in the pediatric clinic until the mother was ready to be discharged from the obstetric department, i.e. for 5-8 days. The mother was allowed to attend to the child herself for the last few days and was given instructions concerning the fixation. Careful instruction to the mother regarding the fixation and its purpose is very important.

The length of the treatment period varied. Generally, in cases of typical sub-

luxation it continued for 3 months (39 cases), but in 13 cases for 4-5 months, and in 5 cases for 1-2 months.

During the child's first three months, fixation on the board was usually satisfactory, but after this age the board was found to be less suitable. The child generally begins to kick more vigorously at about this time, and is more difficult to immobilize. In those cases where fixation was necessary for a longer period than 3 months, a so-called Frejka pillow was used, which consists of a diaper with a pillow and wooden board which is placed between the legs and tied over the shoulders (Fig. 14). I have also tested this method with the newborn, but have found that it is more uncertain for obtaining sufficient flexion and abduction. It is also possible that if the child is not secured firmly enough, it may extend its legs and thus risk relaxation.

In the majority of cases, on examining the stability of the hip joint by subluxation provocation after a few days' fixation treatment, it was found that the hip joint was fixed in its reduced position, so that it was no longer possible, even by



Fig. 14. Frejka's abduction pillow.

firm pressure, to displace the femoral head and provoke any click sign (Palmén 1957). If the child lies with the femoral head fixed in a reduced position, the capsule and muscles adapt their tone according to this position. In a fully reduced position, the femoral head is sucked firmly into the cartilaginous acetabulum, which even in the newborn embraces a large part of the head (4/10 according to Faber).

Since it is possible that this examination of the stability of the hip may be of use in determining the length of the treatment period, some further details concerning cases treated will be given here.

In 51 cases the fixation of the femoral head was tested, as described above, after a period of treatment on the wooden board lasting from a few days to 10–12 days.

Of the 31 cases who had been diagnosed

clinically as subluxations, 23 were completely stable on discharge from hospital after a period of between 4–5 and 11 days. Out of the 8 cases in whom, on discharge, it was still possible to displace the femoral head, the hip joint was found to be completely stable in 4 cases on re-examination about a week later. Four cases, in whom the femoral head could still be displaced easily on discharge from hospital after about a week, were later admitted to the orthopedic clinic. These cases are mentioned below (Nos. 19, 20, 21 and 27).

Of the 20 cases who had exhibited subluxation clinically on provocation, the femoral head could no longer be displaced in 17 cases on discharge from hospital. Three of these were, however, later referred to the orthopedic clinic—these cases are mentioned below (Nos. 18, 22 and 24). The remaining 3 were found to be stable on examination about one or two weeks later.

The fact that the femoral head is firmly fixed in the joint after only a short period of treatment is probably not a *reliable* sign that fixation treatment for a short period is sufficient.

In a few cases, for purposes of study, I gave no treatment, or discontinued fixation when the femoral head was found to be firmly fixed in the joint after about one week.

Some details will be given here of the 5 cases who from the beginning received no treatment, and also of 8 cases who were treated for a very short period.

(1) R. K., boy, 510614. Cousin of his mother had had luxation. Breech delivery. Typical click in left hip joint. Roentgen findings uncertain (Group I, oblique position). No treatment. On later roentgen pic-

tures no capital nucleus was seen on the left side until after 10 months. Follow up examination March 1961 ($9\frac{9}{12}$ yrs.): completely normal hip joints.

(2) A. A., girl, 511126. No known heredity, normal delivery. Typical click left side. Roentgen findings uncertain (Group I, oblique position). No treatment. On roentgen re-examination at 3 months, total luxation seen. Plaster treatment at the orthopedic clinic for 6 months. Follow-up examination February 1961 ($9\frac{3}{12}$ yrs.): completely normal hip joints.

(3) E. P., boy, 520418. Aunt and grandmother had luxation. Brother, born here 1957, subluxation at birth. Normal delivery. Typical click on left side, insignificant on right. Roentgen findings uncertain (Group I, oblique position). No treatment. At 1 month still typical subluxation click on left side; fixation on board 1 month only. Later roentgen examination negative. Follow-up examination February 1961 ($8\frac{3}{4}$ yrs.): completely normal hip joints.

(4) L. G., girl, 561028. No known heredity, normal delivery. Typical click left hip joint. Roentgen—slight subluxation left side (Group II). Fixation on board for 9 days, hip joint then completely stable (femoral head could not be displaced on provocation). On later examinations, nothing abnormal found. Follow-up examination February 1961 ($4\frac{1}{4}$ yrs.): roentgen finding completely normal.

(5) I. L., girl, 561030. No known heredity, normal delivery. Typical click left side. Roentgen—bilateral subluxation (Group II). Fixation on board for 11 days, hip joints then stable. Left capital nucleus developed later than right. Later examinations—nothing abnormal found. Follow-up examination March 1961 ($4\frac{1}{12}$ yrs.). Roentgen—completely normal hip joints.

(6) A. F., girl, 561102. Mother had left luxation. Normal delivery. Typical click left side. Roentgen—uncertain (Group II, oblique position). Fixation on board for 7 days, hip joint then completely stable. Later examinations—nothing abnormal found. Follow-up examination March 1961 ($4\frac{1}{12}$ yrs.). Roentgen—completely normal hip joints.

(7) E. G., girl, 561218. No known heredity for luxation. Foot presentation. On provocation both femoral heads could be displaced posteriorly. Roentgen (Group II)—slight bilateral subluxation. Fixation on board for 9 days, hip joints then completely stable. Re-examination at 7 months—normal position of hip joints, acetabular roof and capital nuclei normal. Did not come for further examinations; died at home at 4 yrs. of laryngotracheitis.

(8) A.-K. H., girl, 570121. Mother has bilateral subluxation (1961). Normal delivery. Left femoral head could be displaced on provocation, roentgen (Group II) revealed left subluxation. Fixation on board for 4 days, hip joint then completely stable. On examination at 5 weeks the femoral head could again be displaced, and fixation was then recommenced and continued for 2 months. At 6 months, normal position, but still no ossified nucleus visible in left femoral head; the right capital nucleus was 7 mm in diameter. Later examinations—nothing abnormal found. Follow-up examination April 1961 ($4\frac{1}{12}$ yrs.). Roentgen—completely normal hip joints.

(9) A.-K. L., girl, 580122. No known heredity for luxation. Normal delivery. Left femoral head could be displaced posteriorly on provocation. Roentgen findings uncertain (Group I). No treatment, as she lay in good abduction without fixation. Later examinations—nothing abnormal found. Follow-up examination February 1961: completely normal.

(10) T. H., girl, 580626. No known heredity for luxation. Normal delivery. Both femoral heads could be displaced on provocation. Roentgen findings uncertain (Group I). Fixation for 4 days, hip joints then completely stable, afterwards lay with the legs in 90° abduction without fixation. Later examinations—nothing abnormal found. Follow-up examination March 1961 ($2\frac{7}{12}$ yrs.). Roentgen—completely normal hip joints.

(11) M. J., girl, 590528. No known heredity for luxation. Normal delivery. Left head could be displaced on provocation. Roentgen examination with extended adducted legs revealed slight subluxation. On inward rota-

tion in 45° abduction with extended legs the head could be very easily felt subluxating, and roentgen examination in this position (Group III) revealed subluxation. No treatment, since she lay, without fixation, in 90° flexion and 90° abduction. Nothing abnormal found during later examinations. Follow-up examination February 1961 (1 $\frac{3}{4}$ yr.). Roentgen—completely normal hip joints.

(12) U.-B. L., girl, 590812. An elderly relative had probable luxation. Normal delivery. Both femoral heads could be displaced on provocation. Roentgen findings uncertain (Group I). Fixation on board for 12 days, hip joints then completely stable. Later examinations—nothing abnormal found. Both capital nuclei were somewhat irregular, and the left had a rather small calcium content. Latest examination in February 1961 (1 $\frac{1}{2}$ yr.). Roentgen—acetabular roof normal, right capital nucleus normal; the left was of the same size but had a rather smaller calcium content (no necrosis).

(13) E. O., girl, 600509. Maternal grandmother had "bad hip joints". Breech delivery. Left femoral head could be displaced on provocation. Roentgen (Group I) revealed left subluxation. Fixation on board for only 2 days, hip joints then completely stable. Later examinations—nothing abnormal found. Normal capital nuclei at 5 months. Last examination, January 1961 (8 months): roentgen examination revealed nothing abnormal.

The 14 cases who for different reasons were referred to an orthopedic clinic, will also be mentioned briefly here.

(14) I.-M. G., girl, 511104. Two distant relatives had probable luxation. Normal delivery. Typical click right side, less marked on left side. Roentgen findings uncertain (Group I, oblique position). Discharged from hospital with a padded splint between the knees. Referred by the local doctor at 1 month to the orthopedic clinic. No definite signs of subluxation were found there, even after arthrography, and the child was dis-

charged wearing a large disposable diaper. Luxation, however, at 4 months; plaster treatment for 5 months. At 11 months there were still no ossified nuclei in the right femoral head, and this later became necrotic. Follow-up examination in March 1961 (9 $\frac{1}{2}$ yrs.): clinically—nothing abnormal found. Roentgen—acetabular roof very satisfactory, no subluxation. Right femoral neck in a slightly varus position, and right capital nucleus somewhat flatter than the left.

(15) R. G., boy, 531003. No known heredity for luxation. Normal delivery. Typical click left side. Roentgen findings uncertain (Group I, oblique position). Treated for 6 months with fixation on a board. At 2 months there was still slight subluxation, which remained at 6 months, and the child was therefore referred to the orthopedic clinic. Plaster applied for 5 weeks, followed by a luxation box. As the left acetabular roof was dysplastic a shelf operation was performed at 3 $\frac{1}{2}$ yrs. Follow-up examination February 1961 (7 $\frac{1}{2}$ yrs.): nothing clinically abnormal found. Roentgen—acetabular roofs very satisfactory, even left side normal. Slightly valgus position of the femoral neck; left femoral head somewhat broader than the right.

(16) K. F., girl, 531222. No known heredity for luxation. Breech delivery. Also had bilateral pes equino-varus. Typical bilateral click. Roentgen (Group I) revealed total bilateral luxation. Fixation on board, but at 4 months luxation still present—was almost certainly never reduced, since the retention was poor. Referred to orthopedic clinic, where a reduced position could not be obtained, and therefore treatment was postponed indefinitely. She later developed a hydrocephalus and died at the age of 1 year 2 months. This case probably belongs to the so-called teratological malformation cases, where the acetabulum is small and shallow from the beginning.

(17) A. R., girl, 540301. No known heredity for luxation. Normal delivery. Typical bilateral click. Roentgen (Group I) revealed bilateral subluxation. Fixation on a board for 3 months. On examination at 9 months

there was uncertainty about a slight subluxation, and she was therefore transferred to the orthopedic clinic. Arthrography revealed that the femoral head was well in against the acetabulum on extension. Since the edge of the limbus did not quite reach down to the Y-line, it was considered that there was a slight subluxation, and treatment continued with a Frejka pillow during the daytime and a luxation box at night. Later roentgen examinations, and follow-up examination January 1961 (7 yrs.): completely normal.

(18) A. J., girl, 561110. No known heredity for luxation. Normal delivery. Left head could be displaced on provocation. Roentgen (Group I) revealed left subluxation. Fixation on board, and after 12 days the head could not be displaced. Abduction treatment 3 months. Left capital nucleus developed later than the right, and became fragmented at 15 months. Transferred to orthopedic clinic: no subluxation, was treated with luxation box at night. Follow-up examination March 1961 ($4\frac{1}{2}$ yrs.): clinically satisfactory, left leg about 1 cm shorter than the right. Roentgen—acetabular roofs normal, no subluxation. Left femoral head and neck are rather broader than right.

(19) A. A., girl, 570404. Cousin of the mother had luxation. Sister, born 1959, had subluxation. Normal delivery. Typical click left side; roentgen (Group I) revealed left subluxation. Fixation on board 3 months. On discharge after 7 days, left head could still be slightly displaced. Did not come again for examination until age of 3 months. Clinically and roentgenologically then satisfactory—nothing abnormal found. At 1 year slight dysplasia of left acetabular roof, and left capital nucleus smaller than right. Examination at the orthopedic clinic—slight dysplasia, no subluxation, luxation box to be used. Follow-up examination February 1961 ($3\frac{10}{12}$ yrs.) clinically nothing abnormal found. Roentgen—still slight dysplasia of acetabular roof, right acetabular angle 19° , left 25° , no subluxation. Capital nuclei of equal size, lateral part of left one somewhat irregular.

(20) G. P., boy, 570528. Paternal aunt had luxation. Paternal grandmother had hip

trouble. Normal delivery. Typical click right hip joint; left femoral head could be displaced. Roentgen findings negative (Group I). Treated on board; on discharge after 7 days the right femoral head could be displaced very easily, and one had the impression of feeling no acetabular roof edge. On examination at 3 months—nothing clinically abnormal found. Roentgen—normal position, still no capital nuclei. Treatment continued. Did not subsequently come for examination before the age of 10 months, because of pertussis. Fixation had been discontinued at 5 months. Dysplastic acetabular roof and right subluxation found. Transferred to orthopedic clinic; plaster treatment for 6 months, followed by luxation box. Follow-up examination February 1961 ($3\frac{8}{12}$ yrs.). Nothing clinically abnormal found. Roentgen—acetabular roof very well developed, right = left, 23° . Capital nuclei a little irregular, but of normal size for his age.

(21) A.-K. S., girl, 570602. No known heredity for luxation. Normal delivery. Typical click left side. Roentgen findings (Group I) uncertain. Fixation on board. On discharge after 10 days the left head could still be displaced. At 1 month: left head subluxates at 45° abduction. Continued fixation on board. Later moved to Stockholm, and at 5 months was examined at an orthopedic clinic there: normal position, luxation box to be used. Later moved to Germany and has been examined at an orthopedic clinic there. Latest roentgen examination, February 1961 ($3\frac{8}{12}$ yrs.): acetabular roof normal, no subluxation, left capital nucleus 2 mm lower than the right, otherwise nothing abnormal found.

(22) M. S., girl, 570704. No known heredity for luxation. Breech delivery. Left head could be displaced posteriorly on provocation. Roentgen findings (Group I) uncertain. Treatment on board; after 5 days hip joint was stable. Fixation for 3 months. At later examinations the position was considered to be normal, but at 16 months there was slight left-sided subluxation. Transferred to orthopedic clinic: plaster for 6 weeks, later luxation box. Follow-up exam-

ination February 1961 ($3\frac{7}{12}$ yrs.): nothing clinically abnormal found. Roentgen—completely normal hip joints.

(23) B.-M. A., girl, 570924. No known heredity for luxation. Normal delivery. Typical click left side. Roentgen (Group I) showed slight left subluxation. Treated on board; after 4 days hip joint completely stable. Fixation for 3 months, and later Frejka pillow. At 7 months left luxation. Transferred to orthopedic clinic, plaster treatment given. Follow-up examination April 1961 ($3\frac{1}{2}$ yrs.). Nothing clinically abnormal found. Roentgen—completely normal.

(24) M. K., girl, 580225. Cousin had a suspected luxation. Normal delivery. Left head could be displaced on provocation. Roentgen (Group I) uncertain. Fixation on board; after 8 days the hip joint was stable. Treated on a board for 4 months. Uncertainty whether the treatment was carried out properly at home, since the mother is somewhat mentally debilitated. At 4 months slight left-sided abduction limitation, dysplastic left acetabular roof and possibly slight subluxation. Transferred to orthopedic clinic: probably slight subluxation on leg extension. Arthrography revealed subluxation of a few mm. Plaster applied for a few months. Found satisfactory on later examinations. Follow-up examination February 1961 (3 years): acetabular roofs have developed normally, completely normal roentgen picture.

(25) B. P., girl, 581211. Two elderly relatives had had luxation. Normal delivery. Typical bilateral click. Roentgen (Group III): left subluxation, right side uncertain. Fixation on board for 3 months. At 4 months suspected left subluxation. Transferred to orthopedic clinic: no definite subluxation. Treated with a von Rosen splint for 1 month, followed by a Frejka pillow. Later examinations—nothing abnormal found. The capital nuclei showed irregular ossification during growth, but no fragmentation. Follow-up examination February 1961 ($2\frac{2}{12}$ yrs.): normal acetabular roof, capital nuclei of normal size, still somewhat irregularly calcified.

(26) L. J., girl, 590131. Three older relatives had luxation. Normal delivery. Typical click right side; left femoral head could be displaced. Roentgen (Group III) showed bilateral subluxation, most marked on right side. Fixation on board, and after 9 days hip joints stable. At 5 months roentgen examination showed suspected subluxation on leg extension. Transferred to orthopedic clinic: no definite luxation, but plaster treatment given, nevertheless, for 5 months. Later examinations—nothing abnormal found. Follow-up examination February 1961 (2 yrs.). Nothing clinically abnormal found. Roentgen—normal hip joints (right capital nucleus insignificantly smaller than left).

(27) L.-L. J., girl, 590708. No known heredity for luxation. Normal delivery. Typical click left side; right side could be displaced. Roentgen (Group III): left subluxation. Fixation on board, but on 7th day the head could still be displaced easily. Discharged to an infant home, and from there transferred to orthopedic clinic at 2 months: nothing abnormal then found. Fixation on board until 4 months old, then a von Rosen splint applied for 3 months, followed by a Frejka pillow for a few months. At later examinations the left capital nucleus was found to have a rather smaller calcium density than the right. Follow-up examination March 1961 ($1\frac{8}{12}$ yr.): acetabular roof normal; left and right capital nuclei of similar size, but still rather less calcium density in left (not fragmented).

The remaining 43 cases, as previously mentioned, were treated on an abduction board for an average period of 3 months, and the treatment in these cases was carried out with ease and without any complications. Roentgenological examinations were made 2-3 times during the first year, and then a few times at longer intervals. Clinical examinations were generally made at 1 and 2 months, and subsequently at the same time as the roentgen examinations.

VI. FOLLOW-UP EXAMINATION OF THE TREATED CASES

Even if the observation period is much too short for any assessment of the final results of the treatment, I will nevertheless mention here the condition of the treated cases at the follow-up examination performed during the months January–March 1961.

To estimate with certainty the final results of treatment of luxation of the hip joint, it is probably necessary to wait until growth is complete, i.e. until the age of 15–20 years. A good idea of the condition may, however, be obtained long before this, and the subsequent development of the joint can also be assessed with a high degree of probability.

If at the age of 3 years the acetabulum is normally developed without any signs of dysplasia, the capital nucleus and the femoral neck are normally developed and there are no signs of subluxation, there are good grounds for assuming that the subsequent development will give an anatomically normal joint.

Even if at this age there are small changes, such as only slight dysplasia of the acetabular roof with an insignificantly greater angle, or if there is still somewhat delayed development of the capital nucleus (rather smaller size and calcium density), but no signs of subluxation, the subsequent development of the joint may nevertheless be quite normal.

A more marked dysplasia of the acetabular roof, a small deformed capital nucleus—the result of fragmentation—and a deformed femoral neck, at about the age of 3 years, indicate that the joint will probably not become anatomically normal, even if at this age there are no signs of dislocation.

Out of the 70 cases in the whole material, 2 died, as mentioned previously (Nos. 7 and 16). One left the country, and I was unable to make follow-up examinations; this case was mentioned previously (No. 21).

All of the other 67 cases treated were examined roentgenologically in 1961 on an especially constructed table (Fig. 15), on to which the child was strapped in a symmetrical position with the hip joints in a position of 30° flexion (to counterbalance the lumbar lordosis) and with the legs in 30° inward rotation (to counterbalance the marked anteversion of the femoral neck, normal during the first years).

Thirty-nine of these 67 cases were at least 3 years old at the follow-up examination. *Thirty-four of these (of whom 25 displayed clinical signs of subluxation at birth and 9 subluxation on provocation) showed a completely normal roentgen picture and even at the clinical examination the hip joints were normal.*

The other 5 cases were those who were

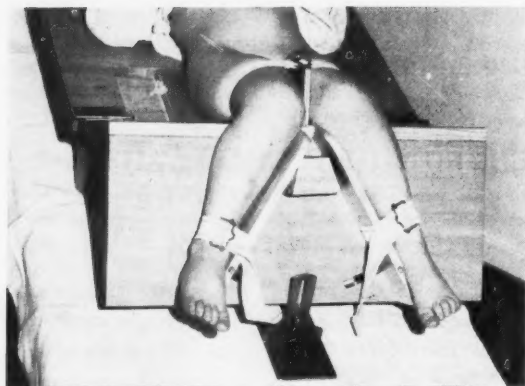


Fig. 15. The table used for the roentgen follow up examination.

treated at the orthopedic clinic and have been mentioned previously (cases Nos. 14, 15, 18, 19 and 20). In none of these cases was subluxation observed. Two cases (Nos. 19 and 20) showed only insignificant roentgenological signs of dysplasia at the follow-up examination at the ages of $3\frac{10}{12}$ yrs. and $3\frac{8}{12}$ yrs. respectively, and it was probable that they would develop normal joints. One case (No. 15) was doubtful, exhibiting at 7 years a moderately valgus position of the femoral neck and a rather broad femoral head. In two cases, (Nos. 14 and 18), the results of capital fragmentation were observed at $9\frac{1}{2}$ years and $4\frac{4}{12}$ years, respectively. The femoral head had nevertheless developed satisfactorily in these cases, and the acetabular roofs were normal.

At the follow-up examination 28 cases were less than 3 years old, and could not therefore be judged with the same degree of certainty. Sixteen cases, however, showed a completely normal roentgen picture (9 had subluxation and 7 preluxation on provoca-

tion). Of the remaining 12 in this group, 11 cases (6 subluxations and 5 subluxations on provocation) still showed slight signs of dysplasia and in one case the capital nucleus had still not ossified. There was no subluxation in any of the cases and no capital fragmentation. The clinical examination revealed completely normal findings in all of these 28 cases.

Results of the Follow-up Examination

Of the first 39 cases, who were at least 3 years old at the follow-up examination, 34 (87.2%) showed completely normal hip joints, clinically and roentgenologically.

Of the remaining 5 cases, none of whom showed signs of subluxation, 2 still had only slight dysplastic changes, and it is probable that they will develop normal joints. The percentage of normal hips will then be 92.3%. 1 had dysplastic changes to a somewhat greater degree, and 2 showed the results of capital fragmentation.

PART II

The Diagnosis of Congenital Dislocation of the Hip Joint in Children in Sweden during the Years 1948-1960

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GENERAL ASPECTS

One of the main purposes of this investigation, as mentioned previously, was to find out whether the diagnosis of preluxation of the hip joint in the newborn can effectively reveal the majority of those cases, which if left untreated might give rise to luxation during childhood years. This should be reflected in the frequency figures for the number of cases of dislocation in childhood, which have been treated at all the orthopedic clinics.

In Sweden there have long been orthopedic clinics in Härnösand for the northern part of the country, in Stockholm for the eastern, in Gothenburg for the western and in Hälsingborg, Lund and Malmö for the southern regions. During the last decade about a further 10 new orthopedic clinics have been added to central hospitals in different parts of the country. It may thus be assumed that practically all cases of dislocation of the hip joint have been treated at orthopedic clinics.

By the kind co-operation of the chiefs of all the orthopedic clinics in the country, I was able to study the case journals of children who were either admitted to hospital or given out-patient treatment for luxation, subluxation or preluxation of the hip joint during the period from 1948–1960.

The secretaries of these clinics looked for the case journals of these children, and attempt was made to include all

cases. I was then able to borrow either the original journals or photostat copies.

Children born abroad to foreign parents were not included. On the other hand, children born in Sweden to foreigners living in this country were included.

All patients born after the 1st January 1940 were included. In this way children with dislocation discovered up to the age of 9–10 years were included for the year 1950. For the later years, those who were treated at orthopedic clinics for the first time *after* the age of 10 years were accordingly excluded. This figure, however, comprised only 21 cases altogether.

Every case was recorded on a card, where not only the age, name, address and name of parents, but also the age at which the dislocation was discovered, and the dates of the first roentgen examination and first treatment were recorded. The cards were classified according to the calendar year during which the first treatment was given at the respective orthopedic clinics.

By a re-classification according to the number of births in the whole material, it was possible to check that no child was recorded in duplicate by being transferred from one clinic to another.

The material was finally found to comprise 1486 cases, 1269 girls and 217 boys ($\text{♀}:\text{♂} = 5.8:1$).

Since the journals often contained no

information concerning the place of birth of the child or the reason for which the hip joints were examined, the parents of those children born after the 1st January 1953 were written to, when necessary, in order to obtain complementary information. By means of information from the journals, inquiries to the parents, and, when no reply was received from them, inquiries to the obstetric clinics possibly concerned, I was finally able to establish the place of birth of the child in 725 out of the 739 cases, born between 1953 and 1960. This information was thus lacking in only 14 cases (1.9 %).

By recording the places of birth in this way, I was able to find out which children

were born at the obstetric clinics where examination of the hip joints was performed on the newborn as routine.

This material from the orthopedic clinics was then compared with another card register of all children who were born between the 1st January 1953 and the end of 1960 and examined at obstetric clinics, and who, during this examination, showed a positive click sign according to Ortolani's method. By the kind co-operation of my pediatric colleagues, who are consultants to obstetric clinics throughout the country, these cases were recorded for this period.

The results of these investigations are shown in Tables 3-7.

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THE MATERIAL FROM ALL THE ORTHOPEDIC CLINICS

This is shown in Table 3, where the cases are grouped according to the calendar year when they first attended the clinic.

It was found that up to and in-

TABLE 3. *No. of cases of dislocation, subluxation and preluxation treated before the age of 10 years at all orthopedic clinics in Sweden during the years 1948-1960.*

A, no. of cases.

B, no. of cases treated as inpatients.

C, no. of cases who could be treated as out-patients.

D, no. of cases who underwent reduction under anesthesia and application of plaster.

E, no. of cases diagnosed at obstetric clinics.

F, no. of cases diagnosed before the age of 2 months (the newborn excluded).

G, no. of cases diagnosed at the age of 2-6 months.

H, no. of cases diagnosed at the age of 6-12 months.

I, no. of cases diagnosed at the age of 1-2 years.

J, no. of cases diagnosed after the age of 2 years.

Year	A	B	C	D	E	F	G	H	I	J
1948	118	116	2	115	0	0	8	8	72	30
1949	103	102	1	100	0	3	6	10	60	24
1950	101	99	2	98	0	2	6	6	50	37
1951	107	107	0	104	1	3	5	6	67	25
1952	120	119	1	117	1	2	7	8	71	31
1953	108	102	6	93	9	1	6	4	64	24
1954	105	102	3	96	15	1	7	9	38	35
1955	105	92	13	86	16	2	5	9	46	27
1956	112	92	20	79	36	3	7	7	38	21
1957	131	84	47	75	65	3	9	6	32	16
1958	147	84	63	83	81	3	6	5	36	16
1959	118	47	71	44	85	0	5	4	16	8
1960	111	49	62	45	73	1	4	4	19	10
Total	1,486				382					

cluding the year 1952 the frequency of those children who had to have in-patient treatment at the clinics comprised almost 100 % of all cases treated. The few cases who did not need to be treated as inpatients were children who were too old for reduction of the luxation to be possible.

From 1953 onwards there was an increasing number of children whom it was possible to treat as out-patients. Practically all of these were newborn children who had been transferred from the obstetric clinics. Thus, during 1959 and 1960, 60 % and 56 % respectively of all children treated at the orthopedic clinics for this disease were able to receive treatment as out-patients.

This is also reflected in the frequency of children who underwent reduction and application of plaster under anesthesia. Before 1953 this figure constituted 97-98 % of the total number of children treated. During 1959 and 1960, however, only 37 % and 41 %, respectively, needed to be treated in this way.

For the years 1948, 1949 and 1950 the material included no children who were diagnosed at birth. There was one case in 1951 and one in 1952, both of whom I diagnosed. From 1953 onwards there was an increasing number of children who were transferred from the obstetric clinics, and in the later years these constituted a large percentage of all the cases treated.

Calendar year	No. of cases treated	% transferred from the obstetric clinics
1953	108	8.3
1954	105	14.3
1955	105	15.2
1956	112	32.1
1957	131	49.6
1958	147	55.1
1959	118	72.0
1960	111	65.8

Before the time when newborn children were transferred to the orthopedic clinics, about 100–120 children were treated there annually for luxation, and, as shown in Table 3, this figure remained about the same during the later years. Thus in spite of the fact that the number of newborn children referred to the clinics did not bring about an increase in the total number of cases treated, *during 1959 and 1960 about two-thirds (69%) of all cases treated at*

the orthopedic clinics were children in whom the diagnosis was made during the first week of life.

The ages of the other children at the time the diagnosis was made may be seen in the table. It is of interest here, that the number of children who were brought for treatment before the age of 1 year, newborn children excluded, is on the whole constant, even during the later years. This shows that the forming of a diagnosis during the first year of life at the child welfare clinics and centres, where about 96% of all newborn are examined (1958), needs to be intensified, so that those cases who pass through the examination at the obstetric clinic without discovery, or who perhaps show no clinical signs until after the age of a few months, may be diagnosed as early as possible.

TABLE 4. *Cases of dislocation, subluxation and preluxation treated at the orthopedic clinics during the years 1953–1960, grouped according to year of birth.*

A, no. of treated cases.
B, no. born at those obstetric clinics included in the investigation.
C, no. born at other obstetric clinics.
D, no. born at home.
E, obstetric place not known.
F, diagnosis made at an obstetric clinic.
G, diagnosis made at those obstetric clinics included in the investigation.
H, diagnosis made at another obstetric clinic.

I, diagnosis made before the age of 2 months, the newborn excluded.
J, diagnosis made at the age of 2–6 months.
K, diagnosis made at the age of 6–12 months.
L, diagnosis made at the age of 1–2 years.
M, diagnosis made after the age of 2 years.
N, no. of cases born at those obstetric clinics included in the investigation in whom preluxation was not discovered at the obstetric clinic, and who were later admitted for subluxation or dislocation.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1953	78	28	47	2	1	13	12	1	0	3	11	39	12	16
1954	86	35	42	4	5	17	17	0	1	5	9	40	14	18
1955	74	31	41	0	2	19	17	2	3	6	6	33	7	14
1956	117	63	48	1	5	41	39	2	3	9	7	45	12	24
1957	111	75	36	0	0	70	61	9	2	8	4	21	6	14
1958	105	78	27	0	0	75	64	11	2	8	3	14	3	14
1959	95	77	17	0	1	75	65	10	1	3	5	11	0	12
1960	73	63	10	0	0	70	61	9	1	2	0	0	0	2
Total	739	450	268	7	14	380	336	44	13	44	45	203	54	114

The number of cases who were not brought for treatment until after the age of 1 year, shows a marked gradual decrease:

Calendar year			Calendar year		
No.	%		No.	%	
1948	102	86.4	1955	73	69.5
1949	84	81.6	1956	59	52.7
1950	87	86.1	1957	48	36.6
1951	92	86.0	1958	52	35.4
1952	102	85.0	1959	24	20.3
1953	88	81.5	1960	29	26.1
1954	73	69.5			

Thus during 1959 and 1960 (without there being any increase in the total number of children treated because of the influx of newborn) *only about one-quarter (23.1%) of the cases of dislocation in children treated at the orthopedic clinics were those who came for treatment after the age of 1 year.* Before the introduction of examination in the newborn this figure was about 85%.

Table 4 shows those children who were treated at the orthopedic clinics during 1953-1960 (the years when examination was being made at the obstetric clinics), grouped according to the year of birth. It is shown here that of these 739 children, 450 were born at those obstetric clinics whose material is included in this investigation, and where routine examination of the hip joints was made on all newborn. Of these 450, 336 (74.7%) showed signs of preluxation during their first week, while 114 (25.3%) showed no signs of dislocation until later. This may appear to be a high "percentage error" for the examination of the newborn, and will be discussed in more detail later.

The table also shows how the number of cases of dislocation who were first treated between the ages of 1 and 2 years became smaller and smaller during the latter years of the investigation period.

Year of birth	Dislocation discovered at 1-2 years
1956	45
1957	21
1958	14

Table 5 shows the reason for which the hip joints were examined in those children born between 1953 and 1960. Those cases in whom the diagnosis was made during the first week of life have not been included here. In a few cases examination was made during the child's first year, after the parents had suspected something wrong with the hips or legs because of an abnormal position, some form of asymmetry, leg shortening, etc.

TABLE 5. The reason for which the hip joints were examined in those cases of dislocation and subluxation treated at the orthopedic clinics during the years 1953-1960.

- A, year of birth.
B, no. of cases.
C, diagnosis made after the parents had sought medical advice during the child's first year for reasons of suspected abnormality of the hip or leg.
D, the parents had sought medical advice after the child's first year, when the child was observed to limp or was late in beginning to walk.
E, diagnosis made at an examination at a child-welfare clinic or centre.
F, diagnosis made at an investigation of congenital malformations.
G, diagnosis made at an examination performed on admission to hospital for another disease.
H, reason unknown.

A	B	C	D	E	F	G	H
1953	65	6	38	7	0	2	12
1954	69	7	46	5	0	3	8
1955	55	3	34	12	2	1	3
1956	76	4	46	11	0	6	9
1957	41	2	23	8	2	4	2
1958	30	4	16	8	0	2	0
1959	20	2	10	3	3	0	2
1960	3	0	0	1	1	1	0
Total	359	28	213	55	8	19	36

The table also shows that strikingly few cases are diagnosed at the routine examinations made at the child welfare clinics and centres. Only 55 (17.0%) of the 323 cases where the reason for the examination is known were diagnosed in this way, in spite of the fact that the great majority of these cases attended the child welfare clinics or centres. These 55 cases also include 10 cases on whom the diagnosis was formed at a routine roentgen examination of girls 4-6 months of age (Berglund 1956).

In 8 cases dislocation of the hip joint

was discovered during an investigation of malformations of the skeletal system.

In 19 cases dislocation was established during a hospital examination for another disease; in some cases as a secondary finding at a roentgen examination of the pelvis for another disease.

A large number of those cases (213—65.9%—out of 323) where the reason for the examination is known, were diagnosed after the age of one year when the parents had sought medical advice because the child limped or was exceptionally late in beginning to walk.

THE MATERIAL FROM THE OBSTETRIC CLINICS

This is shown in Table 6. In 1953 routine examination of the hip joints was introduced by pediatric consultants at 26 obstetric clinics, where approximately one-third of all children in the country were born. The examination has since been adopted in several other clinics, and during the last two years, i.e. 1959-1960, the hip joints of the newborn have been examined at all of the 45 clinics in the country having pediatric consultants. During these years about two-thirds of all children in Sweden were born at these clinics. As may be seen in the table, an increasing number of cases of preluxation of the hip joint have been diagnosed in this way, not only due, however, to the increase in the number of children examined.

During the first few years the frequency of cases diagnosed was about 1%, while during the last three years it has increased to 2.8, 3.2 and 2.7%, respectively.

There was a marked increase after 1957, when my article on the examination and diagnosis in the newborn, published in the Swedish Medical Journal, was sent to all physicians at the obstetric departments and other maternity institutions, together with a memorandum from the National Medical Board, which recommended this examination of the hip joint in all newborn children.

The figures given in Table 6 for the number of children examined, are probably rather uncertain. Those children

who died during the first week of life are excluded, since the majority of these probably had no hip joint examination. On the other hand, the prematurely born children are included, since most of them were transferred to the pediatric clinics and were usually examined there by the same person.

Only those cases were included as preluxations, for whom it was stated that the examination revealed the click sign. Cases of "an uncharacteristic click" or "crepitations" were excluded.

TABLE 6. *Cases of preluxation of the hip joint, diagnosed by the click sign during the first week of life, at obstetric clinics in Sweden from 1953 to 1960.*

- A, no. of children born alive in the whole country (those who died during the 1st week (1.03-1.21 %) are excluded).
B, no. of newborn examined.
C, % no. of group A examined.
D, no. of cases of preluxation of the hip joint diagnosed; ($\varnothing : \sigma = 4.1 : 1$).
E, frequency of preluxation cases diagnosed as % of the number examined.
F, no. of newborn transferred to orthopedic clinics.

Year	A	B	C	D	E	F
1953	108,811	33,681	31.0	32	1.0	12
1954	103,833	38,064	36.7	44	1.2	17
1955	106,079	42,301	39.9	41	1.0	17
1956	106,690	47,520	44.5	76	1.6	39
1957	105,891	50,942	48.1	113	2.2	61
1958	104,383	66,394	63.6	187	2.8	64
1959	103,569	68,570	66.2	216	3.2	65
1960	101,038	68,070	67.4	185	2.7	61
Total	840,294	415,542	49.5	894	2.2	336

TABLE 7. *Cases of dislocation and subluxation treated at the orthopedic clinics from 1953-1960, who were born at the obstetric clinics included in the investigation, but where preluxation had not been diagnosed.*

- A, year of birth.
 B, no. of cases of dislocation and subluxation.
 C, % of the number of newborn examined.
 D, no. of cases of preluxation diagnosed at those obstetric clinics which are included in the investigation.
 E, the ratio of cases of later occurring dislocation and subluxation to the number with preluxation.

A	B	C	D	E
1953	16	0.48	32	1:2.0
1954	18	0.47	44	1:2.4
1955	14	0.33	41	1:2.9
1956	24	0.51	76	1:3.2
1957	14	0.27	113	1:8.1
1958	14	0.21	187	1:13.4
1959	12	—	216	} Observation period as yet too short
1960	2	—	185	
Total	114		894	

The increase in frequency from 1957 onwards may be also partly connected with the fact that in a number of clinics, subluxation provocation was also introduced into the examination of the hip joints at that time. In these clinics the frequency was then 5-6%.

In compiling this material, the only intention was to show the frequency of cases of preluxation, which have been diagnosed in this way in Sweden. This series of cases was not studied in respect to roentgen examination or treatment. It should just be mentioned here that a large number of these 894 cases diagnosed were treated with the abduction position, approximately according to those principles followed in the treatment of my cases.

In those hospitals where there are orthopedic clinics, cases were transferred to these clinics at the beginning, and a number of cases were sent to nearby orthopedic clinics. The total number of cases transferred to orthopedic clinics is 336 (37.6%).

By comparing the material from the obstetric clinics with that from the orthopedic clinics, I was able to find out how many cases who were left untreated because of "negative" roentgen findings were later admitted to orthopedic clinics for subluxation or dislocation. There were found to be 30 such cases.

Finally, Table 7 shows those children born at the obstetric clinics whose material is included in the investigation, in whom preluxation was not diagnosed, but who were later admitted to orthopedic clinics for luxation. These cases, 114 in all, are mainly distributed, taken as a percentage of the number of newborn examined, into the first 4 years, and the large number of cases then undiscovered at birth is almost certainly not representative of the reliability of the examination of the newborn. During the first years there was less interest in the examination in a number of clinics, and it was found that the frequency of cases diagnosed increased with the years when interest and experience became greater.

It must also be mentioned here that in several clinics no record was made in the case journals of whether or not the hip joints were examined, and only positive findings were noted. In only 30 cases was a record made in the case journal from the obstetric clinic, that the hip joints had been examined and were found to be normal. In the remaining 84 cases no record

of a hip joint examination was made. It was thus not possible to establish with certainty whether all of the 114 cases were actually examined as newborn children. Ten of them were transferred to a pediatric clinic after birth, because of prematurity or illness (e.g. asphyxia, malformations), and examination of the hip joint was possibly not performed there at once.

Two of the 114 cases were born in Falköping and showed as newborn at my examination no symptoms of preluxation. One showed the click symptom at the age of 2 months while the other was not diagnosed until it was 2 years of age, when it was observed to be limping. This child had never attended the child welfare clinic.

It was considered of interest to obtain somewhat more certain figures concerning the possibility, by means of examination of the hip joints of all newborn children, of diagnosing as preluxation those cases who could otherwise be expected to have luxation later in childhood. Since my own material was too small for this purpose, I made some calculations on the series of cases examined at the obstetric clinics in Gothenburg and Malmö. Examination of the hip joints have been performed on the newborn at these clinics since 1953, and there are also orthopedic clinics in these towns. Pediatricians and orthopedists there have shown great interest in these examinations.

The number of newborn examined at the obstetric clinics in Gothenburg and Malmö during the years 1953-1958 was 53,585 (35,144 and 18,441 respectively). Of these, 109 cases (80 and 29 respectively) of preluxation (2.0 %) were diagnosed by the "click sign". (During 1959 and 1960, 59 cases (3.2 %) were diagnosed out of 18,182 examined, an increase probably

due to the introduction of subluxation provocation).

The calculated number of cases of subluxation and dislocation during the first years of childhood, out of the 53,585 examined, is 48 (0.9% according to Severin 1956).

The number of cases of later diagnosed subluxation and dislocation born in the years 1953-1958 at these obstetric clinics and admitted to the orthopedic clinics during the years 1953-1960, is 7 (5 and 2, respectively). These constitute 14.6 % of the 48 cases who are expected to have subluxation or dislocation.

Since there had been an observation period of at least 2 years even for the children born in 1958, and since during 1959-1960 no cases diagnosed after the age of 2 years were admitted to these orthopedic clinics for subluxation or luxation, the figure of 7 can be considered as representative.

In none of these 7 cases was a record made in the case journals from the obstetric clinic of whether or not the hip joints had actually been examined. Two cases were transferred after birth to the pediatric clinic, one because of asphyxia, the other because of malformations; there was no record of whether or not the hip joints were examined. It may thus be presumed that in some of these 7 cases no examination of the hip joints was made, and the percentage figure of 14.6 then becomes lower.

There is no doubt that with careful examination of the hip joints in the newborn, following the principles mentioned, it should be possible to diagnose at least 90 % of those cases of preluxation, which left untreated might be expected to give rise to subluxation or dislocation during childhood.

PART III

Summarizing Discussion and General Summary

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SUMMARIZING DISCUSSION

As has been partly indicated in the introduction, the views on the causation of congenital dislocation of the hip joint, its occurrence and development, have been divergent, and many different theories have been suggested. I shall not describe these in detail; only those ideas prevailing at the present time will be discussed.

The general opinion is that in the great majority of cases, about 98 %, dislocation occurs because of a congenital "dysplasia", a defect in the normal development of the hip joint, and perhaps also of its surrounding tissues.

Much has been written concerning heredity; the influence of this factor cannot yet be regarded as clear. In most reports the examiner has concluded that a hereditary cause for luxation is present in about 25-30 % of the cases. This is based, however, on the case histories. Information that a relative has limped, even if he has done so since childhood, cannot be taken as definite proof that he has had luxation. It is probably more important, however, that there are no doubt many cases not previously diagnosed, who were hitherto free of symptoms or whose symptoms had been so slight that there had been no reason to consult a doctor. Only roentgen examination of the family members and relatives can thus give a more definite idea concerning heredity. The only investigation of this kind which I have found in the literature, is that pub-

lished by Faber (1936 and 1937). He made roentgen examinations in Leipzig of the hip joints of all the members of ten families, in each of which there was a case of luxation. This investigation, which comprised over 400 people, revealed 25 cases of dislocation and 73 further cases of dysplasia (shallow acetabulum). No hereditary sex differences were found, and with only one exception (a rather uncertain case), the hereditary tendency came from only one of the parents. Faber therefore considered the disease to follow a dominant hereditary pattern. It is, further, of interest that in this material the incidence of dislocation was five times greater in females, while in cases of dysplasia the predilection for the female was only 1.7 times that for the male.

In my material, out of the 70 cases, probable dislocation in relatives was revealed by the case histories in 23 (= 33 %), of which 16 were cases with subluxation, and 7 cases which were diagnosed by means of subluxation provocation. In 4 cases siblings had had luxation, and in 2 cases the mother.

Much has been written previously about intrauterine causes of dislocation, e.g. abnormal foetal position, especially the breech position. A higher frequency of breech deliveries than normal deliveries has long been observed among luxation cases. This may possibly be due to the fact that if there is a tendency to preluxation,

this is more liable to become manifest at birth as subluxation, if the child has lain in a breech position, because of the *in utero* stretching of the joint capsule in this position.

In my series of 70 cases, 8 (11.4 %) were breech deliveries. Out of the 12,394 newborn examined 230 (1.9 %) were born in breech presentation. Preluxation occurred about 6.8 times as often in those children born in the breech position as in those born in a cephalic presentation.

In a few percent of cases, the luxation is caused by a malformation of the acetabulum, which is small and shallow, and the femoral head is also small and deformed. These cases, which are thus etiologically different from the majority of cases, have long been known, and have been named, as suggested by Le Damany (1908), "teratological luxation". The luxation is often combined with other malformations, such as club foot, luxation of the knee joint, spinal deformities, arthrogryphosis multiplex, and chondroosteodystrophy. There was one such case (No. 16) in my series, and 27 cases (1.8 %) in the material from the orthopedic clinics. These cases are as a rule very difficult to treat, and usually on reduction there is extremely poor retention of the femoral head in the shallow acetabulum.

Finally, it should be mentioned that dislocation of the hip joint occurs in a large number of cases of cerebral palsy with spasticity of the legs, especially in severe cases where there has been considerable prolonged contracture of the adductor muscles. Brodin (1961) reported that out of 48 mentally backward children with cerebral palsy, who at a certain period were being cared for at an institu-

tion, no fewer than 27 had subluxation or luxation. In such cases dislocation is not congenital and there is no preluxation at birth.

Ortolani, *inter alia*, showed by arthrography and pathologo-anatomical investigations that in cases of subluxation the cartilaginous acetabulum may be normally developed at birth and during the first months of life. With arthrography it may be observed on the roentgen film that the limbus goes right down to the Y-line. In a few cases Ortolani has found that the posterior-superior part of the cartilaginous acetabulum is somewhat more poorly developed at the age of a few months. This may be due to secondary changes which may occur at an early stage by the pressure exerted by the femoral head against this part of the acetabulum, even in a slight subluxation. Experimental dislocation of hips in animals gives secondary dysplasia (Langenskiöld and Sarpio 1957 and Smith *et al.* 1958).

An interesting theory concerning the etiology of dislocation has recently been put forward by Andrén (1960). He has demonstrated that dislocation in the newborn is combined with an abnormal instability in the symphysis pubis. If a roentgenogram, taken with the hip joints in 90° abduction and with traction on each leg laterally, is compared with one taken in the same position but with the femoral head pushed into the acetabulum, there is a difference of at least 2 mm in the width of the symphysis pubis in cases of dislocation, and in some cases of up to 7 mm. Normally this difference is seldom as much as 2 mm and is usually only about 1 mm.

Andrén considered this instability to

depend on a hormonal disturbance, and Andrén and Borglin (1960 and 1961) have since demonstrated an increased excretion of oestrone and oestradiol 17β in the urine during the first four or five days of life in newborn children with dislocation. The administration of oestradiol to these cases also results in an increased excretion of the above hormones compared with normal newborn children. The authors consider that these investigations support the view that "congenital dislocation of the hip is caused by an inborn and probably inherited error of the metabolism of oestrogens".

The Subsequent Development of those Cases, Which at Birth Exhibit Preluxation with or without Subluxation

The question arises here concerning the possibility of spontaneous recovery. A number of cases of spontaneous recovery from luxation in children during the first year of life have been described in the older literature. In a detailed study of those cases reported, for whom roentgen pictures were published, Faber (1939) found that in 66 cases, all of whom had subluxations, the roentgen picture after "spontaneous recovery" showed a certain degree of subluxation remaining in a number of the cases, and a dysplastic acetabular roof in several more cases. The majority of the cases were described after much too short an observation period. Even if it is a common experience among orthopedists, that spontaneous recovery of subluxation can occur (e.g. Wiberg 1939), this is nevertheless very rare. In the majority of cases a subluxation develops into an increasing degree of luxation, and in a

number of cases complete luxation can occur within a few months (e.g. case No. 2). But in other cases the subluxation may remain without giving rise to any clinical symptoms until much later in childhood, or until adult years are reached.

In cases of subluxation the ossification of the femoral head and acetabular roof often occurs considerably more slowly than in a normal joint, even if treatment with the abduction position is commenced immediately. It has been possible to observe this at roentgen examinations in many of the cases I have treated. If a subluxation is not treated from the beginning, the abnormal position doubtless prevents the normal development of the hip joint, which, especially during the first months of life, is rapid and important. A correct position of the femoral head in the acetabulum probably also acts as an inducement to the normal growth in the joint.

The physiological increase in tone in the adductor muscles, which occurs after a few weeks, when the child, instead of lying, as at the very beginning, with the legs in flexion-abduction, begins to kick more and to lie with extended legs, causes the femoral head to press more and more up against the weaker, posterior-superior part of the acetabulum. This appears to encourage luxation, as does also the body weight, when the child later begins to stand.

Because of the displacement of the femoral head with increasing luxation, the joint mechanics become changed, and a number of the changes which are found at a later stage are considered to be due to this alteration in mechanics, e.g. the increased valgus position of the femoral neck and increased anteversion (Exner, 1954).

The high frequency of preluxation found in the newborn by the use of the examination methods described exceeds, as has been previously shown, the frequency of luxation in children, found earlier. The question therefore arises:

Is the Diagnosis Made Too Frequently in the Examinations of the Newborn?

This is a question of fundamental importance, and will be discussed in more detail here. It may be asked, whether the displaceability in the hip joint, which may be found by means of subluxation provocation, is actually an expression of a preluxation. Is it perhaps only a "physiological flaccidity" which does not require any treatment?

For the following reasons I am convinced that this increased laxity, which permits a manual subluxation, is in fact an expression of a preluxation of the same type as that where subluxation already exists at birth:

(a) Those cases in whom it is possible to provoke subluxation are, after all, rather few; in my own material there are 24 cases out of 5700 examined (4.2%). In the overwhelming majority of cases it is thus not possible to displace the femoral head in the newborn, even if strong pressure is exerted. This cannot be done even immediately after death in the newborn, when there is complete flaccidity.

(b) Probable cases of luxation were recorded in the case histories of 7 (29%) out of the above-mentioned 24 cases, approximately the same frequency as in the subluxation material, 16 (34.8%) out of 46 cases.

(c) In two cases (Nos. 22 and 24), in

spite of the fact that treatment was commenced immediately, plaster treatment was later required for slight subluxations. In a third case (No. 18), capital fragmentation occurred.

(d) In 7 cases the capital nucleus developed later in unilateral preluxation, and was for a varying period smaller than on the other side.

(e) As mentioned in the report on the roentgen examination, this revealed subluxation in 12 cases out of 19 cases of preluxation, diagnosed by subluxation provocation.

(f) In 10 cases, who exhibited a typical click sign on the one side, the contralateral femoral head could be displaced on provocation.

These cases thus hardly differ in any respect from those where a subluxation click can be demonstrated at birth. They possibly represent only a "small degree" of preluxation.

Since some of these cases probably develop normal joints without any treatment, the question arises:

Should Treatment Be Commenced Immediately Even in All Such Cases of "Slight" Preluxation?

The fact that normal joints may be developed is demonstrated by two cases from my series (Nos. 9 and 11), whom as an experiment I left untreated, since at the beginning they lay, without fixation, with the hip joints in 90° flexion and abduction.

In several cases a very short period of fixation treatment is sufficient: 5 cases were secured in an abduction position for only 2-12 days (Nos. 7, 8, 10, 12 and 13), and normal hip joints were found at the

follow-up examination. In one of these (No. 8) where the fixation was discontinued after 4 days, when the femoral head was stable, it was found necessary, however, to recommence treatment at 5 weeks, when the head could again be displaced.

It should be mentioned here that, even in a few cases with a typical subluxation click, it was possible to limit the treatment in the same way to a similarly short period, and even one untreated case showed normal joints at the follow-up examination (see cases Nos. 1, 3, 4, 5 and 6).

It is obvious, therefore, that a number of cases can improve spontaneously, and others require only very short periods of fixation treatment. In my experience, however, it is not possible to decide with certainty, either by a clinical or roentgen examination, which cases are likely to recover spontaneously or need treatment for only a very short period. Therefore, in my opinion, treatment with the abduction position should be commenced as soon as a preluxation with or without subluxation is diagnosed in a newborn child. In those cases in whom slight displaceability of the femoral head or a slight subluxation click are found at the clinical examination, and where the femoral head is completely stable after about a week of treatment, one may perhaps be content with such a short period of treatment. It is important however in these cases to follow up the development of the joint by re-examinations to check that subluxation has not occurred. Future experience will also perhaps give a better idea of the length of the treatment period required.

By treating all cases from the beginning, even those with an apparently "mild degree" of preluxation, it may be

possible to reduce the frequency of those cases of slight subluxation which do not show symptoms until later in childhood or until an adult age is reached. Since the number of cases diagnosed at the obstetric clinics exceeded so markedly the frequency of luxation during childhood years, previously known, it is conceivable that a large number of these cases are in fact those with slight preluxation.

It has long been considered that arthrosis deformans (osteo-arthritis) in the hip joint in adults is to a great extent caused by congenital subluxation, which in many cases may not be manifest until adult years. Putti (1933) found subluxations in 40 % of a series of cases with arthrosis deformans.

In follow-up examinations of patients with subluxation and dysplastic acetabulum, Wiberg (1939) was able to compare the roentgenograms before and after the occurrence of osteoarthritis, in 19 cases, and was thus able to show very clearly the relationship between these conditions. He also found that in 25 % of a material of osteoarthritis, this disease was originally due to subluxation.

The view that the treatment of even mild cases of preluxation in the newborn may be good prophylaxis against that form of arthrosis deformans in the adult which is caused by congenital subluxation, has also been put forward earlier by Hart (1950) and Chiari (1953).

The treatment of the newborn was, as has been mentioned, commenced with fixation on a wooden board, and this method has also been used in many other places. von Rosen (1956) has used an aluminium splint (Fig. 16), and considers

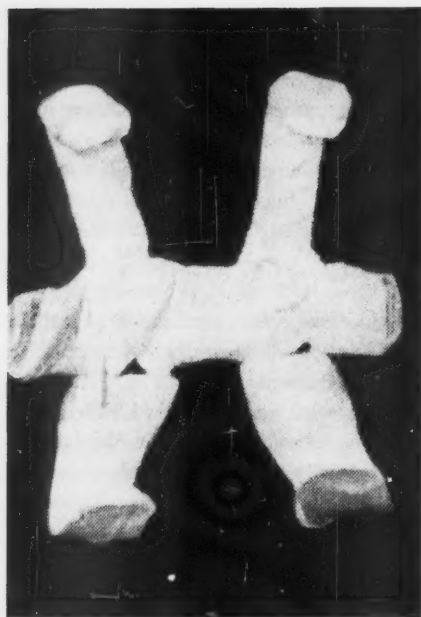


Fig. 16. von Rosen's aluminium abduction splint (from von Rosen (1956)).

it more suitable than the wooden board, giving, in his opinion, better fixation and thereby reducing the risk of capital fragmentation. According to von Rosen, this risk increases if the femoral head is allowed to move in and out in the joint during nursing care. As I have mentioned previously, in using the wooden board the nursing staff and the mothers were given instructions that when the board was removed for changing the baby, the legs should not be extended or adducted. As early as after one or two days on the board, the child lies with the legs in 90° abduction, even if the board is removed. Moreover, in the majority of cases fixation of the hip joint occurs after only a week, preventing luxation.

A form of fixation which permits a certain degree of movement in the hip joints is probably most favourable for the development of the joint (Severin 1957).

Fragmentation of the femoral head occurs mainly after reduction under anesthetic, and subsequent to fixation with plaster bandages. A report published by Chiari (1953), who treated 198 cases at the ages of 3 weeks to 3 months, is of interest in this connection. Muscular contracture had developed in many cases, and 49 cases had to be reduced under anesthetic; in 21 of these (43%), there were marked changes in the femoral head. Among the remaining 149 cases, in whom reduction was made without anesthetic and who were easily placed in the abduction position,

femoral head changes occurred in only 8 cases (5.4%). At the same time Chiari reports that 274 cases, who were diagnosed before the age of 3 weeks, could be placed with ease in the abduction position on a plaster shell and secured with an elastic bandage. At a re-examination of 249 of these cases, complete recovery was found, without changes in the femoral head. Twenty cases, whose treatment had not been completed, returned later with luxation.

This evidence is good support for the view that when preluxation is diagnosed in the newborn, treatment should always be commenced immediately.

In the main, only the initial treatment in the newborn has been discussed here. The subsequent treatment that is required will not be discussed here. That is more purely an orthopedic question. The experience gained from cases treated early is moreover not extensive enough as yet for any categoric rules to be laid down as to the most suitable form of treatment.

To conclude, a few further aspects of the roentgen examination of the newborn will be discussed.

As has been previously described, it is usually possible to reveal a subluxation by using different methods of roentgen examination. This is, however, in my opinion, only a confirmation of that which can be established at the clinical examination; if a typical click is produced with Ortolani's manoeuvre, this means that a subluxation is present. Even in those cases where a preluxation can be diagnosed only by means of subluxation provocation, a roentgen picture can reveal subluxation. For the roentgen photograph, however, the legs must then be held in a

position where it may be felt clinically that the femoral head is subluxated, e.g. the position used by Andrén and von Rosen. In the requirements for the roentgen examination, stated by these authors, they give as point 1: "The femora should be kept dislocated during the exposure of the film".

Since according to the view put forward here all cases of preluxation in the newborn should be treated as early as possible, and since a roentgen examination of the newborn does not provide any information concerning the degree of severity of the preluxation, in my opinion there is no reason for examining these cases roentgenologically before the commencement of treatment. *The diagnosis of preluxation in the newborn is a clinical and not a roentgenological matter.* The experience gained in Sweden up to the present time, as reflected in the pediatric and orthopedic material which I have studied, also shows that roentgen examination of these newborn children is of no value. During the last few years the orthopedic clinics have all adopted the policy of commencing treatment immediately in those cases which show obvious symptoms on clinical examination.

It is important, however, later in the treatment period, to check by roentgen examination that the subluxation has been reduced, and that the joint is developing normally. In my opinion the first roentgen examination ought to take place at about the age of 2-3 months, and always before the discontinuation of fixation treatment.

In the material from the obstetric clinics, which I studied, the result of the roentgen examination performed was in

many cases judged as "negative" or "uncertain". A number of these cases in different parts of the country were therefore left untreated. The material from the orthopedic clinics, however, included 30 such cases who were later admitted for luxation. It must, of course, be pointed out that the roentgen examination was perhaps not carried out sufficiently carefully in these cases, but this does show that in practice the clinical examination is more reliable than the roentgen.

It has long been considered that by means of a roentgen examination of all newborn children it should be possible to discover any dislocations present, but this has not led to any positive results. Caffey *et al.* (1956) reports that in 666 children who underwent roentgen examinations when newborn and again at the age of 6 months, 2 exhibited subluxation at the later examination, which had not been observed on the first occasion. The

measurement of the acetabular angle and the investigation of the degree of abduction and the skin folds in the newborn in this material also gave such uncertain results, that Caffey wrote: "We seriously question that predislocation of the hip during early infancy actually exists as a recognizable clinical entity."

In Sweden Berglund (1956) examined roentgenologically 1099 infants at the age of about 4 months. He reported that out of these, 3 showed luxation. The disadvantage of this method is that at 4 months, the most favourable time for the commencement of treatment, i.e. the neonatal period, has been missed. Moreover, a number of dislocations may not be manifest until after the age of 4 months. There are also considerable organizational difficulties in obtaining all children for such an examination, and much expense is involved.

GENERAL SUMMARY

Since 1950 the author has examined the hip joints of all newborn, i.e. 12,394 children, at the obstetric clinic of the Central Hospital in Falköping, using the abduction manoeuvre described by Ortolani, which from 1956 onwards has been complemented with a subluxation provocation. Up to and including 1960, 70 cases with positive symptoms were diagnosed in this way. These were treated immediately with fixation in an abduction position on a wooden board. The method of examination and the treatment are described.

At a re-examination in 1961, out of 39 cases who were at least 3 years old, 34 (87.2 %) showed clinically and roentgenologically normal joints. In the remaining 5 cases the continued development of the joint will probably be normal in a further 2. The percentage of normal hips will then be 92.3 %. One case had dysplastic changes to a somewhat greater degree, and two showed results of capital necrosis. Their future development is at present uncertain.

The cases thus diagnosed are regarded as representing a stage of preluxation in the newborn. Left untreated, a number of these cases may heal spontaneously, and others may give rise to subluxation or luxation during the first to second year of life, in milder cases not until later in childhood, or adult years in the form of arthrosis deformans (osteoarthritis).

A critical study is made of the roentgen

examination of the newborn, and in particular its sources of error. This examination revealed nothing in cases of preluxation in addition to that which could be established clinically. Roentgen examination of these cases before the commencement of treatment is therefore considered unnecessary.

An examination of a normal material of newborn was made in respect to the possible degree of abduction in the hip joints and the symmetry of the skin fold on the medial side of the thigh. All had an abduction of at least 70°. Only 39.6 % had symmetrical thigh folds. 27.6 % had no folds at all, these being mainly children with a low birth weight. Asymmetry of the skin folds thus does not appear to be a symptom of value in the diagnosis.

Most cases of preluxation have normal abduction, and many have increased flaccidity of the joint.

At the suggestion of the author the examination of the hip joints was introduced in January 1953 into the routine examination of all newborn children at the majority of obstetric clinics having pediatric consultants. Up to and including 1960 approximately 415,500 newborn children were examined, constituting 49.5 % of all children born alive in Sweden during this period. During 1959 and 1960 approximately 67 % were examined. This material was analyzed. Altogether 894 cases of preluxation were diagnosed

(=2.2%). During the later years this frequency was about 3%. In those clinics which also used the subluxation provocation method in the examination during the later years, the frequency was about 5-6%. No obvious geographical differences in the frequency within Sweden was found in this material.

In order to study how the diagnoses made at the obstetric clinics have affected the frequency of luxation during later childhood, and thereby the usefulness of this diagnosis, all cases of luxation of the hip joint in children treated at the orthopedic clinics in Sweden during the years 1948-1960, 1486 cases altogether, were recorded. (In Sweden practically all cases of luxation are treated at orthopedic clinics.) The ages of the children at the time the diagnosis was made, and the reasons leading to the examination of the hip joints, are given.

During the later years an increasingly large number of newborn children were transferred to the orthopedic clinics, but in spite of this there was no marked increase in the number of cases treated annually at these clinics.

Approximately 62% of the preluxation cases were treated at the pediatric clinics, the majority as out-patients.

Of the cases of luxation admitted to orthopedic clinics during the years 1948-1950, none had been diagnosed when newborn, and 85% were not diagnosed until after the age of 1 year. 97% underwent the customary prolonged treatment with plaster.

Of the 229 cases treated during the years 1959-1960, 69% were diagnosed at obstetric clinics, and only 23% after the age of 1 year. It was possible for 58%

to be treated as out-patients, with a simple method of fixation in an abduction position for a period, in the majority of cases, of only a few months. 39% were treated with plaster.

The material from the orthopedic clinics was compared with that from the obstetric clinics, and in the cases of luxation from the orthopedic clinics, inquiry was made as to the obstetric clinic at which the child was born. It was thereby found that during the years 1953-1960, 114 children were admitted, who were not diagnosed as preluxations when newborn, but who were born at those clinics where the hip joints were examined as routine. Ten cases had been transferred to a pediatric clinic because of prematurity, asphyxia or malformations, and had possibly therefore had no hip joint examination immediately. It was not possible to verify with certainty whether all of the other cases had been examined when newborn.

An obvious tendency was observed in the number of cases of later manifested luxation which was not discovered in the neo-natal period, to decrease with the years, when the interest and experience of the examiners had extended.

The material from those clinics which have shown especial interest and have considerable experience, reveals that at least 90% of those dislocations which may be expected to occur during later childhood years, can be diagnosed as preluxations during the first week of life. In this way they are also available for immediate treatment with simple fixation in the abduction position, and in probably at least 90% the subsequent development of the joint is completely normal.

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This investigation has been carried out at the Central Hospital in Falköping, and I extend my sincere thanks to my colleagues and also the nurses and secretaries at the pediatric and roentgenological clinics for their valuable assistance.

I would like to offer special thanks to the chief of the roentgen department, Dr. Olof Holm, for the great interest which he has shown in my work from the beginning, and for his great help with the roentgenological part of the work.

I would also like to express my appreciation for their help to my colleagues in all the pediatric clinics in the country, who allowed me to examine the data concerning those cases of preluxation diagnosed in the course of their duties as consultants to the obstetric clinics, and many of whom, by valuable discussions, imparted to me much of their experience.

My sincere thanks are also due to the chiefs of all the orthopedic clinics in the country, for placing at my disposal the case journals of those cases of luxation treated at these clinics. I would also like to thank

the secretaries of these clinics for all their help.

I would also like to express here the gratitude which I feel towards the late Professor Erik Severin, former chief of the orthopedic clinic in Gothenburg. For several years he followed my work on these problems, which he had very much at heart, with the greatest interest and kindness, and gave me good advice and encouragement.

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APPENDIX

SUGGESTIONS FOR THE DIAGNOSIS AND TREATMENT OF PRELUXATION IN THE NEWBORN

(1) All newborn should be examined with Ortolani's abduction manoeuvre and by subluxation provocation. The examination should be repeated in a few days, especially (a) if there is luxation in the family or among relatives (a note regarding any heredity for luxation should be made in the mother's case journal when her history is taken), (b) if the child is born in the breech position, (c) if there are any malformations present (pes equino-varus, luxation of the knee joint, spina bifida etc.) or joint contractures (arthrogryphosis multiplex). In all such cases with malformations roentgen examination of the hip joints should be made.

(2) The result of the hip joint examination should be recorded in the case journal; this should also be noted in the report to the child-welfare clinic.

(3) On positive examination findings the child should be transferred to a pediatric or orthopedic clinic for the commencement of treatment.

(4) The treatment should be commenced with fixation of the hip joints in 90°-110° flexion and 80°-90° abduction, on a suitable fixation device. N.B.: It is important to be convinced that the femoral head is reduced in the fixed position, i.e. that it has moved forwards in the "click" examination.

(5) If the child is admitted as an in-patient to the clinic, a test by subluxation provocation should be made on discharge to see whether the femoral head is fixed in the joint.

(6) The mother should be given careful instructions regarding the fixation device, and the principles of the treatment should be explained to her.

(7) The child should be re-examined at about the age of 1 month: (a) the degree of abduction should be tested (unilateral limited abduction should arouse suspicion of subluxation), (b) any asymmetry should be observed (leg shortening, lateral or cranial displacement of the trochanteric region), (c) examination should be made in respect to whether the femoral head can be displaced on subluxation provocation. (d) on suspicion of dislocation a roentgen examination should be made. N.B.: symmetrical alignment of the pelvis is important when taking the roentgen photograph.

(8) If at birth there was only positive subluxation provocation with slight displaceability of the femoral head, or very slight displacement with the click symptom, and if after the commencement of treatment the femoral head is quickly fixed, the fixation treatment may be discontinued after a few weeks.

(9) Re-examination should be made at 2-3 months in the same way as in point 7. Roentgen examination in a symmetrical position.

(10) If the clinical and roentgenological examinations show normal conditions, the treatment may be discontinued. If the hip joint is very flaccid with considerably displaceability of the femoral head at the first examination, or if the

roentgen examination reveals delayed ossification of the femoral head or a sloping acetabular roof, the treatment should probably be continued for a few months.

Finally, since it cannot be assumed that the hip joint examination of the newborn is 100 % effective, the hip joints should also be examined during the routine examinations at the child-welfare clinic.

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